Memo/Agenda
Minutes
Re-Review Summaries
  Alpha Hydroxy Acids
  Sodium Alpha-Olefin Sulfonates
  Polyvinyl Alcohol

CIR EXPERT PANEL MEETING
MARCH 17-18, 2014
MEMORANDUM

To: CIR Expert Panel Members and Liaisons  
From: Director, CIR  
Subject: 130th Meeting of the CIR Expert Panel — Monday and Tuesday, March 17-18, 2014  
Date: February 24, 2014

Enclosed are the agenda and accompanying materials for the 130th CIR Expert Panel Meeting to be held on March 17-18, 2014. This is our first meeting at the Washington Court Hotel, 525 New Jersey Avenue, NW, Washington, DC 20001. Phone: (202) 628-2100. Fax: (202) 879-7993. The meeting agenda includes consideration of 16 ingredient groups advancing in the process and 3 re-review summaries.

At the Panel’s request, CIR invited 2 speakers, Dr. Kayoko Matsunaga and Dr. Surinder Chahal, to provide presentations to the Panel and to discuss the Panel’s questions on hydrolyzed wheat protein and hydrolyzed wheat gluten. Dr. Matsunaga is Professor and Chairperson of the Department of Dermatology at the Fujita Health University School of Medicine, Japan, and Chair of the Japanese Society of Allergology’s Special Committee for the Safety of Protein Hydrolysates in Cosmetics. Dr. Chahal is Director of Research and Technology at Sun Care & Biotechnology, Croda Europe Ltd, Widnes Cheshire, England. The Council made arrangements for an interpreter for Dr. Matsunaga to be available during the presentation and the Team discussions. To accommodate the time allotted for the interpreter, the plan is to have the Teams address hydrolyzed wheat protein as early as possible.

Schedule and hotel accommodations

We have reserved rooms for the nights of Sunday March 16 and Monday, March 17, at the Washington Court. If you encounter any travel problems, please contact me on my cell phone at 410-299-0777.

Team meetings

Draft reports - there are 8 draft reports for review.

1. Alkoxy Polysiloxanes (agenda and flash drive name – polysiloxanes) – This is the first time that the Panel is seeing this report, which addresses 111 ingredients. A Scientific Literature Review was announced for public comment on December 2, 2013. Unpublished data and concentration of use data received from the Council have been incorporated into the report. Do we need more data or can we proceed to issue a tentative report?

2. Citrus-Derived Ingredients (agenda and flash drive name – citrus) - This is the first time that the Panel is seeing this report, which addresses 198 ingredients. A Scientific Literature Review was announced for public comment December 3, 2013. Unpublished data received from the Council have been incorporated into the report. Industry and RIFM questioned the grouping of all citrus-derived ingredients into one report, having stated that the composition of these ingredients is highly variable. Limited information was received on a few of the ingredients. Do we need more data or can we proceed to issue a tentative report?
3. Hydroquinone (agenda and flash drive name – hydroquinone) – At the March 2013 meeting, the Panel decided to reopen the safety assessment of hydroquinone and p-hydroxyanisole and combine them into one report. In December 2013, the Panel decided to table the combined report for the purpose of collecting more data on the use of UV nail lamps. In 2010, the Panel confirmed their conclusion that hydroquinone is safe for use in nail adhesives. Although both ingredients are used for the same purpose in nail products, after further examination, CIR staff decided that the reviews would be conducted separately because the initial reviews, done as individual ingredients, have different safety conclusions. Data submitted have been incorporated into the appropriate report. Are the data sufficient to determine safety of these ingredients individually and for this new use?

4. p-Hydroxyanisole (agenda and flash drive name – p-hydroxyanisole) - At the March 2013 meeting, the Panel decided to reopen the safety assessment of hydroquinone and p-hydroxyanisole and combine them into one report. In December 2013, the Panel decided to table the combined report for the purpose of collecting more data on the use of UV nail lamps. In 2003, the Panel confirmed that p-hydroxyanisole was unsafe for use in cosmetic products because of the potential for skin depigmentation. Although both ingredients are used for the same purpose in nail products, after further examination, CIR staff decided that the reviews would be conducted separately because the initial reviews, done as individual ingredients, have different safety conclusions. Data submitted have been incorporated into the appropriate report. Are the data sufficient to determine safety of these ingredients individually and for this new use?

5. Inorganic Sulfates (agenda and flash drive name – inorganic sulfates) – This is the first time that the Panel is seeing this report, which addresses 17 ingredients. A Scientific Literature Review was announced for public comment on December 2, 2013. Unpublished data received from the Council, and updated sensitization data on persulfates, have been incorporated into the report. Do we need more data or can we proceed to issue a tentative report?

6. Methylisothiazolinone (MI) (agenda and flash drive name – methylisothiazolinone) – At the March 2013 meeting, the Panel decided to reopen the safety assessment of this ingredient. Since the final safety assessment of MI was issued in 2008 (published in 2010), new clinical data indicate a higher than expected frequency of individuals who have allergic reactions to the preservative MI. Relevant data from the public literature and concentration of use data from the Council have been incorporated into the report. Do we need more data or can we proceed to issue a tentative report?

7. PEG-150 Pentaerythrityl Tetrastearate (agenda and flash drive name – PEG-150 pentaerythrityl) – This is the first time that the Panel is seeing this report addressing this single ingredient. The Scientific Literature Review Notice was issued on December 2, 2013. Technical comments from the Council have been addressed and unpublished data were added. Do we need more data or can we proceed to issue a tentative report?

8. Tripeptide-1, Hexapeptide-12, and Related Amides (agenda and flash drive name – palmitoyl oligopeptides) – At the March 2013 meeting, the Panel decided to table the report for the purpose of focusing on ingredients for which the peptide sequence is known, i.e., tripeptide-1, hexapeptide-12, and specific related amides. This focus is also consistent with the new definitions for palmitoyl oligopeptides in the INCI Dictionary. Data submitted have been incorporated into the report. Are more data needed or can we proceed to issue a tentative report?
Tentative reports – there are 2 draft tentative reports.

1. Camellia Sinensis-Derived Ingredients (agenda and flash drive name – *camellia*) – At the December 2013 meeting, the Panel issued an insufficient data announcement on the safety of camellia sinensis-derived ingredients. The Panel requested method of manufacturing and composition data; concentration of use; and an HRIPT on the leaf (100%), stem/leaf extract (3%), and catechins. The Panel also requested confirmation that the leaf water is only used as a fragrance and information on the difference between leaf oil and leaf essential oil. Data submitted have been incorporated into the report. No data on the method of manufacture were submitted. Technical comments have been considered. If the information is still insufficient, then a tentative conclusion of insufficient data should be issued. If the information now available is sufficient, the Panel should issue a Tentative Report with an appropriate discussion and conclusion.

2. Fatty Acid Amidopropyl Dimethylamines (agenda and flash drive name – fatty acid dimethylamines) – At the September 2012 meeting, the Panel tabled the report to allow for the consideration of data from additional studies on stearamidopropyl dimethylamine which are being prepared under the auspices of the REACH program. The Panel also determined that the data were insufficient to support the safety of the fatty acid amidopropyl dimethylamine ingredients. The Panel requested percutaneous absorption data on cocamidopropyl dimethylamine, and if absorbed, reproductive and developmental toxicity data, and sensitization and irritation data on oleamidopropyl dimethylamine at use concentrations. Data received from industry on an irritation study of 1% oleamidopropyl oil and summary data from the ECHA database have been incorporated into the report. Technical comments have been considered. If the information is sufficient, the Panel should issue a Tentative Report. If the information is still insufficient, the Panel should issue a Tentative Report with an insufficient data conclusion.

Final reports - there are 6 draft final reports for consideration. After reviewing these drafts, especially the rationales provided in the discussion section, the Panel should issue them as final reports.

1. Alkyl Betaines (agenda and flash drive name – alkyl betaines) – At the December 2013 meeting, the Panel concluded that these ingredients are safe in the present practices of use and concentration in cosmetics when formulated to be non-irritating. No new data were received. Technical comments from the Council were considered.

2. Hydrolyzed Wheat Protein and Hydrolyzed Wheat Gluten (agenda and flash drive name – hydrolyzed wheat protein) – At the September 2013 meeting, the Panel concluded that these ingredients are safe for use in cosmetics when formulated to minimize peptide lengths greater than 30 amino acids. Additionally, these ingredients should not be used on damaged skin or in products that may come in contact with mucous membranes or may be incidentally inhaled. No additional new unpublished data were received. Technical comments, such as the request that information on non-hydrolyzed wheat gluten be included in this report and that the Panel consider a re-review of the safety of Triticum Vulgare (wheat) protein and germ protein, have been considered.

3. Monosaccharides, Disaccharides, and Related Ingredients (agenda and flash drive name – saccharides) – At the December 2013 meeting, the Panel concluded that these ingredients are safe in the present practices of use and concentration in cosmetics. Calcium gluconate has been added as an ingredient in this safety assessment. Oral exposure toxicokinetics data and information on ingredients that are nutritive and non-nutritive sweeteners and/or food additives have also been added. Technical comments from the Council were considered.
4. Pentaerythritol Tetra-Di-t-Butyl Hydroxyhydrocinnamate (agenda and flash drive name – hydroxyhydrocinnamate) – At the December 2013 meeting, the Panel concluded that this ingredient is safe in the present practices of use and concentration in cosmetics. No new data were received. Technical comments received from the Council were considered.

5. Rosmarinus Officinalis (Rosemary)-Derived Ingredients (agenda and flash drive name – rosmarinus) – At the December 2013 meeting, the Panel concluded that 8 ingredients (rosmarinus officinalis (rosemary) extract; rosmarinus officinalis (rosemary) flower/leaf stem extract; rosmarinus officinalis (rosemary) flower/leaf stem water; rosmarinus officinalis (rosemary) leaf; rosmarinus officinalis (rosemary) leaf oil; rosmarinus officinalis (rosemary) leaf powder; rosmarinus officinalis (rosemary) leaf water; and rosmarinus officinalis (rosemary) water) are safe as used in cosmetics; and that rosmarinus officinalis (rosemary) leaf extract is safe at concentrations up to 0.2% in leave-on products, and is safe as used in rinse-off products. Data were insufficient for determining that rosmarinus officinalis (rosemary) flower extract is safe for use in cosmetics. Updated concentration of use data have been added to the report. Technical comments have been addressed.

6. Tocopherols and Tocotrienols (agenda and flash drive name – tocopherols) – At the December 2013 meeting, the Panel issued a tentative amended report with a safe as used in cosmetics conclusion for these 14 ingredients. At the Council’s request, an Epidemiology section has been added to the report, discussing the ongoing debate about the health benefits of vitamin E. Some new information has been incorporated, including information on tocopherol regulatory proteins. Technical comments from the Council have been addressed.

Full Panel Meeting

Remember, the breakfast buffet will open at 8:00 am and the meeting starts at 8:30 am on day 1 and day 2.

The Panel will consider the 6 reports to be issued as final safety assessments, followed by the rest of the reports advancing in the process, and finish with a discussion of the 2015 Priorities.

The bulk of the agenda is the draft reports, but there are almost as many final reports. We also have a number of re-review summaries and two guest speakers. It is still likely that the full Panel session will conclude before lunch on day 2, so plan your travel accordingly.

Have a safe journey.
Agenda
130th Cosmetic Ingredient Review Expert Panel Meeting
March 17-18, 2014

Monday, March 17

8:00 am CONTINENTAL BREAKFAST

8:30 am WELCOME TO THE 130th EXPERT PANEL TEAM MEETINGS

8:40 am PRESENTATIONS

10:15 am TEAM MEETINGS

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Dr. Marks’ Team

FR (CB)  hydrolyzed wheat protein
FR (WJ)  hydroxyhydrocinnamate
DR (WJ)  inorganic sulfates
DR (WJ)  palmitoyl oligopeptides
DR (WJ)  PEG-150 pentaerythrityl
TR (LB)  camellia
DAR (LB)  hydroquinone
DAR (LB)  p-hydroxyanisole
DR (LB)  polysiloxanes
RRsum (LG)  PVA, α-olefin sulfonates, AHAs
FR (MF)  rosmarinus
FR (MF)  saccharides
FR (MF)  tocopherols
FAR (MF)  tocopherols
DR (CB/MF)  citrus

Dr. Belsito’s Team*

FR (MF)  rosmarinus
FR (MF)  saccharides
RRsum (LG)  PVA, α-olefin sulfonates, AHAs
FR (WJ)  hydroxyhydrocinnamate
DR (WJ)  inorganic sulfates
DR (WJ)  palmitoyl oligopeptides
DR (CB)  methylisothiazolinone
DR (CB)  citrus
DAR (CB)  fatty acid dimethylamines
DAR (LB)  hydroquinone
DAR (LB)  p-hydroxyanisole
DR (LB)  polysiloxanes

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Noon Lunch for Panel, liaisons, and staff

2:00 pm Team meetings - continue as needed

5:00 pm ADJOURN DAY 1 SESSION

FR: Final report
FAR: Final amended report
TR: Tentative report
TAR: Tentative amended report
DR: Draft report
RR: Re-review

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.

* Team moves to breakout room.
Tuesday, March 18

8:00 am  CONTINENTAL BREAKFAST
8:30 am  WELCOME TO THE 130th FULL CIR EXPERT PANEL MEETING
8:45 am  Admin  MINUTES OF THE SEPTEMBER 2013 AND DECEMBER 2013
          EXPERT PANEL MEETING  Dr. Bergfeld
9:00 am  DIRECTOR’S REPORT  Dr. Gill
9:30 am  FINAL REPORTS, REPORTS ADVANCING TO THE NEXT LEVEL, RE-REVIEWS, and OTHER DISCUSSION ITEMS

**Final Reports**

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<th>Report</th>
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<td>Alkyl betaines</td>
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<td>FR (CB)</td>
<td>Hydrolyzed wheat protein</td>
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<td>FAR (LB)</td>
<td>Hydroxyhydrocinnamate</td>
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<td>Dr. Gill</td>
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**Reports Advancing**

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**Re-reviews**

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**New Data**

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**ADJOURN** - Next meeting *Monday and Tuesday, June 9-10, 2014*

FR: Final report
FAR: Final amended report
TR: Tentative report
TAR: Tentative amended report
DR: Draft report
RR: Re-review

**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 TWENTY-NINTH MEETING

OF THE

EXPERT PANEL

December 9, 2013

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
Halyna Breslawec, Ph.D.

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

Adopted (Date)

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

Robe Azn
Jay Ansell
Yutaka Aoki
Lillian Becker
Ivan Boyer
Christina Burnett
Kapal Dewa
Monice Fiume
Kevin Fries
Lillian Gill
Rebecca Guenard
Bart Heldreth
Carla Jackson
Wilbur Johnson, Jr.
Dennis Laba
Thomas Re
Mark Reimers
Diego Rua
Doug Schoon
Kevin Sheron
Noriko Shibuya
Sunil Sirdesai
Larry Steffler
David Steinberg
Jeremy Wong

FDA
PCPC
Kanebo
CIR
CIR
CIR
CIR
FDA
CIR
CIR
CHF
CIR
CIR
CIR
Presperse
L’Oreal
Avon Products
FDA
Schoon Scientific
KRP
Shiseido
OPI Products
KRP
Steinberg & Associates
Estee Lauder
CHAIRMAN’S OPENING REMARKS

The 129th meeting of the CIR Expert Panel (combined meeting of Teams and full Panel) was called to order by Dr. Wilma Bergfeld at 8:45 a.m. on Monday, December 9, 2013. Due to inclimate weather, both Team meetings and the full Panel meeting occurred on the same day. Some of the Panel members were in attendance, while others participated via teleconference. Dr. Bergfeld noted that 17 ingredient reports are being reviewed at this meeting, including 7 final reports, 4-re-reviews, and 4 new draft reports.

Dr. Bergfeld noted the need to discuss the use of data supporting the generally recognized as safe (GRAS) status of food additives (some of which are also cosmetic ingredients) in CIR reports. She added that CIR has adopted the practice of including ingredient data from the European Chemicals Agency (ECHA) in CIR safety assessments. Dr. Bergfeld also mentioned the need for the Panel to consider the restrictive conclusion of safe as used in cosmetic products, when formulated to be non-sensitizing and confirm that this language should be incorporated into report conclusions when warranted. Furthermore, she noted that the conclusion of safe as used when formulated to be non-irritating is currently being used.

APPROVAL OF MINUTES

Approval of the minutes of the September 9-10, 2013 CIR Expert Panel meeting was inadvertently overlooked. Approval will be addressed at the March 18 CIR Expert Panel meeting.

DIRECTOR’S REPORT

Dr. Gill thanked the Panel members, staff and attendees for braving the weather to attend the meeting in Washington D.C. Despite some flight delays and cancellations, all Panel members attended, including four members available by teleconference. Because the weather forecast for the full Panel meeting predicted 3-5 additional inches of snow, the Panel agreed to accelerate Team reviews and convene the full session after lunch on the first scheduled day of the meeting. The schedule change resulted in postponing the presentation and subsequent discussion on the infant skin resource document, which Dr. Gill stated would be rescheduled in 2014.

She discussed two additional presentations to be scheduled for early 2014. Dr. Matsunaga, Professor and Chairperson of the Department of Dermatology at the Fujita Health University School of Medicine, Japan; and Chair of the Japanese Society of Allergology’s Special Committee for the Safety of Protein Hydrolysates in Cosmetics has tentatively accepted the CIR invitation to address the Panel at the March 2014 meeting. The Council provided this recommendation at the request of the Panel. This request was prompted after discussion at the September 2013 meeting of reports from Japan of type 1 hypersensitivity reactions to personal care products containing hydrolyzed wheat protein or hydrolyzed wheat gluten.

Dr. Gill also provided an update on CIR’s plan for the assessment of algae ingredients. The CIR agrees with the Science and Support Committee (CIR SSC) recommendation that the SLR on various algae extracts be postponed until the Industry has an opportunity to present additional information from outside experts on the family of algae ingredients. Additionally, since the INCI committee is in the process of changing the trade names associated with the INCI name Algae Extract, the CIR SSC suggested that it may be prudent to wait for the results of that effort.

Lastly, Dr. Gill reminded Panel meeting attendees of the change in meeting location for 2014. All of the 2014 Panel meetings will be held at the Washington Court Hotel, 525 New Jersey Avenue, NW, which is near Union Station. She also announced that beginning January 2, CIR will be located at 1620 L Street, NW. This new location is around the corner from the current office.

Final Safety Assessments

*Achillea millefolium*-derived ingredients

The Panel issued a final amended safety assessment with the conclusion that the three *Achillea millefolium*-derived ingredients listed below are safe as cosmetic ingredients in the present practices of use and concentration described in the safety assessment when formulated to be non-sensitizing.
achillea millefolium extract
achillea millefolium flower/leaf/stem extract
achillea millefolium flower extract

These ingredients may function in cosmetics as skin-conditioning agents – miscellaneous, skin-conditioning agents – humectants; and fragrance ingredients. Achillea millefolium extract was reported to be used in 135 cosmetic products, including 83 leave-on products up to 0.04% and 47 rinse-off products up to 0.03%. There were no uses reported for achillea millefolium flower extract and achillea millefolium flower/leaf/stem extract, but were they to be used in the future, the expectation is that they would be used in product categories and at concentrations comparable to achillea millefolium extract.

The Panel stressed that there may be an accumulation of constituents of allergenic or other toxicological concern (e.g., hydroquinone, linalool) when multiple botanical ingredients containing these constituents are used in the same final product formulation. The Panel also reiterated that all botanical ingredients can contain pesticide residues and heavy metals as impurities, and that the cosmetics industry should continue to use good manufacturing practices to limit these impurities in the ingredient before blending into cosmetic formulations.

Alumina and Aluminum hydroxide
The Panel issued a final safety assessment with the conclusion that alumina and aluminum hydroxide are safe in the present practices of use and concentration in cosmetics.

Alumina was reported to be used in 523 leave-on products at concentrations up to 60%, and in 40 rinse-off products at concentrations up to 30%. Aluminum hydroxide was reported to be used in 572 leave-on products at concentrations up to 10.1% and 6 rinse-off products at concentrations up to 8.8%.

The Panel based their determination on the published safety data, and on the FDA safety review that determined alumina to be safe for use in medical devices (i.e., replacement hips and dental implants). The Panel also considered the FDA’s approval of aluminum hydroxide in over-the-counter drugs (i.e., antacids) and alumina as a color when used in medical devices (i.e., sutures and bone cement).

The Panel reviewed data concerning the ongoing scientific debate about the potential connection of aluminum exposure to Alzheimer’s disease and breast cancer. They concluded that these speculations were not relevant to alumina and aluminum hydroxide because these cosmetic ingredients are not the same as elemental aluminum. Use of alumina and aluminum hydroxide in cosmetics would not result in significant systemic exposure to aluminum.

Amino Acid Alkyl Amides
The Panel issued a final safety assessment with the conclusion that the 115 amino acid alkyl amides listed below are safe in the present practices of use and concentration in cosmetics when formulated to be non-irritating.

- acetyl arginine*
- acetyl cysteine
- acetyl glutamic acid*
- acetyl glutamine
- acetyl histidine*
- acetyl methionine
- acetyl proline*
- acetyl tyrosine
- capryloyl collagen amino acids*
- capryloyl glycinpe
- capryloyl gold of pleasure amino acids*
- capryloyl keratin amino acids*
- capryloyl pea amino acids*
- capryloyl quinoa amino acids*
- capryloyl silk amino acids*
- cocoyl glutamic acid
- dipalmitoylesteine*
- dipotassium capryloyl glutamate
- dipotassium undecylenoyl glutamate*
- disodium capryloyl glutamate
- disodium cocoyl glutamate
- disodium hydrogenated tallow glutamate
- disodium N-lauroyl aspartate*
- disodium lauroyl glutamate
- disodium malyl tyrosinate
- disodium stearoyl glutamate
- disodium undecylenoyl glutamate*
- lauroyl arginine
- lauroyl collagen amino acids
- lauroyl glutamic acid*
- lauroyl lysine
- lauroyl proline
- lauroyl silk amino acids
- magnesium palmitoyl glutamate
myristoyl glutamic acid*
oleoyl tyrosine
palmitoyl alanine*
palmitoyl arginine*
palmitoyl collagen amino acids
palmitoyl glutamic acid*
palmitoyl glycine
palmitoyl gold of pleasure amino acids*
palmitoyl isoleucine*
palmitoyl keratin amino acids
palmitoyl millet amino acids*
palmitoyl oat amino acids*
palmitoyl pea amino acids*
palmitoyl proline
palmitoyl quinoa amino acids*
palmitoyl silk amino acids
potassium caproyl tyrosine*
potassium capryloyl glutamate*
potassium cocooyl glutamate
potassium cocooyl glycinate
potassium cocooyl rice amino acids*
potassium lauroyl collagen amino acids*
potassium lauroyl glutamate*
potassium lauroyl oat amino acids*
potassium lauroyl pea amino acids*
potassium lauroyl silk amino acids*
potassium lauroyl wheat amino acids
potassium myristoyl glutamate
potassium undecylenoyl glutamate*
propionyl collagen amino acids*
sodium caproyl proline*
sodium capryloyl glutamate*
sodium cocooyl alaninate
sodium cocooyl amino acids
sodium cocooyl apple amino acids
sodium cocooyl barley amino acids*
sodium cocooyl collagen amino acids
sodium cocooyl glutamate
sodium cocooyl glutamininate*
sodium cocoyl glycinate
sodium cocoyl/hydrogenated tallow glutamate*
sodium cocoyl oat amino acids*
sodium cocoyl/palmoyl/sunfloweroyl glutamate*
sodium cocoyl proline*
sodium cocoyl threoninate*
sodium cocoyl wheat amino acids*
sodium hydrogenated tallowoyl glutamate
sodium lauroyl aspartate
sodium lauroyl collagen amino acids*
sodium lauroyl glutamate
sodium lauroyl millet amino acids*
sodium lauroyl/myristoyl aspartate*
sodium lauroyl oat amino acids
sodium lauroyl silk amino acids*
sodium lauroyl wheat amino acids
sodium myristoyl glutamate
sodium oliveoyl glutamate*
sodium palmitoyl proline
sodium palmylooyl glutamate
sodium stearyl glutamate
sodium/TEA-lauroyl collagen amino acids*
sodium/TEA-lauroyl keratin amino acids*
sodium/TEA-undecylenoyl collagen amino acids*
sodium undecylenoyl glutamate*
stearoyl glutamic acid*
stearoyl leucine*
TEA-cocoyl alaninate
TEA-cocoyl glutamate
TEA-cocoyl glutamininate*
TEA-hydrogenated tallowoyl glutamate*
TEA-lauroyl collagen amino acids
TEA-lauroyl glutamate
TEA-lauroyl keratin amino acids*
TEA-lauroyl/myristoyl aspartate*
undecylenoyl collagen amino acids
undecylenoyl glycine
undecylenoyl phenylalanine
undecylenoyl wheat amino acids*
zinc lauroyl aspartate*

*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 determined that the available data support the safety of these ingredients under present practices of use and concentration in cosmetics. The Panel considered the function of these ingredients as skin and hair conditioning agents and surfactants, and concluded that they should be formulated to be non-irritating.

In the absence of adequate characterization of the methods of manufacturing, the Panel stated that industry should manufacture amino acid alkyl amides in a way that minimizes the production of residual peptides.

The Panel was concerned about levels of free diethanolamine (DEA) that could be present as an impurity in the ingredients containing triethanolamine (TEA), and stated that the concentrations of free DEA must not exceed those considered to be safe by the Panel (i.e., 0.64%), as stated in the current report on DEA. The Panel cautioned that these ingredients should not be used in cosmetic products in which N-nitroso compounds can be formed.
**Anthemis nobilis-Derived Ingredients**

The Panel issued a final safety assessment with the conclusion that the following four anthemis nobilis flower-derived ingredients are safe in the present practices of use and concentration in cosmetics when formulated to be non-sensitizing:

- anthemis nobilis flower extract
- anthemis nobilis flower oil
- anthemis nobilis flower powder*
- anthemis nobilis flower 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.

Additionally, the Panel reiterated that all botanical ingredients can contain pesticide residues and heavy metals as impurities, and that the cosmetics industry should continue to use good manufacturing practices to limit these impurities in the ingredient before blending into cosmetic formulation.

The Panel reviewed composition data on Anthemis nobilis flower, the flower oil, and the whole plant and determined that these data enabled reasonable assumptions about the composition of the remaining anthemis nobilis-derived ingredients. The Panel expressed concern that cosmetics containing these ingredients may contain potentially sensitizing levels of constituents, such as sesquiterpene lactones. The levels of potentially sensitizing constituents in these ingredients can vary (depending on plant growth conditions, extraction methods, and other factors), and the data available from sensitization tests may not represent the complete spectrum of concentrations of such constituents in the ingredients as used in cosmetic products. Because final product formulations may contain multiple botanical ingredients, each containing potentially sensitizing constituents of concern, formulators are advised to be aware of these constituents and to avoid reaching levels that may be hazardous to consumers. The Panel affirmed that cosmetics containing these ingredients should be formulated to be non-sensitizing.

**Chamomilla recutita-Derived Ingredients**

The Panel issued a final safety assessment with the conclusion that the five Chamomilla recutita-derived ingredients listed below are safe in the present practices of use and concentration in cosmetics when formulated to be non-sensitizing.

- chamomilla recutita (matricaria) flower
- chamomilla recutita (matricaria) flower extract
- chamomilla recutita (matricaria) flower powder
- chamomilla recutita (matricaria) flower water
- chamomilla recutita (matricaria) flower oil

The available data are insufficient for determining the safe use in cosmetics for the following six Chamomilla recutita-derived ingredients:

- chamomilla recutita (matricaria) extract
- chamomilla recutita (matricaria) flower/leaf extract
- chamomilla recutita (matricaria) flower/leaf/stem extract
- chamomilla recutita (matricaria) flower/leaf/stem water
- chamomilla recutita (matricaria) leaf extract
- chamomilla recutita (matricaria) oil

The Panel reviewed new skin irritation and sensitization data on facial cleansing and makeup remover towelettes containing 0.01% chamomilla recutita (matricaria) extract and a hair gel styling mist containing 0.00006% chamomilla recutita (matricaria) flower/leaf extract, but agreed that the available data remain insufficient for evaluating the safety of ingredients from the whole plant, stem, or leaf in cosmetic products. The Panel reiterated that their insufficient data determination is based on the need for composition data on ingredients derived from Chamomilla recutita leaf, stem, or the whole plant.

The Panel expressed concern that cosmetics containing Chamomilla recutita-derived ingredients may be sensitizing because the levels of potentially sensitizing constituents in the ingredients (e.g., sesquiterpene lactones) can vary (depending on plant growth conditions, extraction methods, and other factors), and the data available from sensitization tests may not represent the complete spectrum of concentrations of such constituents in the ingredients as used in cosmetic products. Because final product formulations may contain multiple botanical ingredients, each containing potentially sensitizing constituents of concern, formulators are advised to be aware of these constituents and to avoid reaching levels that may be hazardous to consumers. The Panel also emphasized that final product formulations containing Chamomilla recutita-derived ingredients should meet all applicable or relevant and appropriate International Fragrance Association (IFRA) limits and guidelines established for the constituents of concern.
Formic Acid and Sodium Formate

The Panel issued a final amended safety assessment with the conclusion that formic acid and sodium formate are safe in the present practices of use and concentration in cosmetics when formulated to be non-irritating. Formic acid functions as a pH adjuster, preservative, and fragrance ingredient and sodium formate functions as a preservative in cosmetic products. In 1995, the Panel issued a final report with the conclusion that formic acid is safe when used in cosmetic formulations as a pH adjuster, with a 64 ppm limit for the free acid.

The Panel noted that formic acid is a dermal and ocular irritant, and that any safety concerns relating to the use of formic acid as a preservative or fragrance ingredient would depend primarily on the concentration of free formic acid in the formulation. Neutralized formic acid used as a preservative in cosmetic products would be present predominantly as sodium formate, which has little, if any, potential to cause adverse local or systemic health effects. Furthermore, the Panel agreed that, given the low use concentration of formic acid in leave-on products (i.e., 0.2% in aerosol hair sprays; tonics, dressings, and other hair grooming aids; and non coloring hair preparations), the skin irritation potential of this ingredient in product formulations would not be a concern. The remaining uses of formic acid and sodium formate are at low concentrations in rinse-off products, and these uses would also minimize any concerns relating to skin irritation potential in product formulations.

Phytosterols

The Panel issued a final safety assessment with the conclusion that the 26 phytosterols listed below are safe as cosmetic ingredients in the present practices of use and concentration.

- brassica campestris (rapeseed) sterols
- canola sterols*
- C10-40 isoalkyl acid phytosterol esters*
- dihydrophytosteryl octyldecanoate*
- euterpe oleracea sterols
- glycine soja (soybean) sterols
- persea gratissima (avocado) sterols
- phytosterols
- phytosteryl butyrate*
- phytosteryl canolate
- phytosterol caprylate/caprate*
- phytosteryl hydroxystearate*
- phytosteryl isostearate
- phytosteryl linoleate*
- phytosteryl linoleate/linolenate*
- phytosteryl macadamiate
- phytosteryl nonanoate*
- phytosteryl oleate
- phytosteryl rice branate
- phytosteryl ricinoleate*
- phytosteryl sunflowerseedate*
- punica granatum sterols*
- beta-sitosterol
- beta-sitosteryl acetate*
- soy sterol acetate
- tall oil sterol

*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.

Phytosterols occur naturally as free alcohols and as fatty acid esters. They exist naturally in plant-based foods and are consumed regularly in the diet. The Panel considered the possibility of estrogenic activity and concluded that there was no relevant activity of concern.

The functions of these ingredients include: skin-conditioning agents, hair conditioning agents, viscosity increasing agents, skin protectants, antioxidants, and fragrances. These ingredients are used up to 8%.

Tentative Safety Assessments

Alkyl Betaines

The Panel issued a tentative safety assessment on alkyl betaines with the conclusion that the 11 ingredients listed below are safe in the present practices of use and concentration in cosmetics when formulated to be non-irritating.

- betaine
- behenyl betaine
- cetyl betaine
- coco-betaine
- decyl betaine*
- lauryl betaine
The Panel considered the available data on alkyl betaines and noted low systemic toxicity at high doses in single-dose and repeated-dose oral animal studies, no teratogenic or carcinogenic effects in animal studies, no genotoxicity in in vitro and in vivo studies, and no sensitization in multiple tests. The Panel noted that most surfactants exhibit some irritancy, as was noted in dermal and ocular studies of coco-betaine, lauryl betaine, and a betaine analog. Thus, the Panel stated that products that include these ingredients should be formulated to be non-irritating.

The Panel noted that there were no data available on the UV absorption or phototoxicity of alkyl betaines; however, because none of the molecules that comprise these ingredients are chromophores, the Panel felt that there was no concern that these ingredients would cause adverse effects from UV exposure.

The Panel expressed concern about the dangers inherent in using animal-derived ingredients (i.e., tallow), namely the transmission of infectious agents. They stressed that these ingredients must be free of detectable pathogenic viruses or infectious agents (e.g., bovine spongiform encephalopathy (BSE)). These ingredients should be produced in accordance with good manufacturing practices and should conform to regulations for producing substances from animal-derived materials.

Monosaccharides, Disaccharides, and Related Ingredients

The Panel issued a tentative safety assessment with the conclusion that the following 25 monosaccharides, disaccharides, and related ingredients are safe as used in cosmetics:

- calcium gluconate
- fructose
- fucose*
- galactose*
- galactosyl fructose*
- galacturonic acid*
- gluconic acid
- glucose
- isomalt
- kefiran
- lactitol
- lactose
- lactulose*
- maltose
- mannose
- melibiose
- potassium gluconate
- rhamnose
- ribose
- sodium gluconate
- sucralose
- sucrose
trehalose
- xyllobiose
- xylose

*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 determined that calcium gluconate should be included in this safety assessment. In addition, the Panel determined that the original name of the assessment, “Monosaccharides and Disaccharides as Used in Cosmetics,” should be changed to “Monosaccharides, Disaccharides, and Related Ingredients as Used in Cosmetics”.

The Panel discussed irritation results from a human repeated insult patch test of a hair product that contained 29% sucrose, diluted to 50%. The Panel determined that the irritation was attributable to a surfactant effect, and not to sucrose.

The Panel noted that not all of the ingredients included in this report are GRAS ingredients. However, those products used around the mucous membranes at concentrations as high as 65% are GRAS. Although oral data were not found for the non-GRAS ingredients, the Panel concluded that it was unlikely that these large molecules would get through the skin and, therefore, they had no concerns about the use of these ingredients in cosmetics.

The Panel also agreed with the Industry’s request to add oral exposure toxicokinetics data to the report.
Pentaerythritol Tetra-**di-t-**Butyl Hydroxyhydrocinnamate

The Panel issued a tentative safety assessment with the conclusion that pentaerythritol tetra-di-t-butyl hydroxyhydrocinnamate is safe in the present practices of use and concentration in cosmetics.

Current use concentration data indicate that pentaerythritol tetra-di-t-butyl hydroxyhydrocinnamate is used in leave-on products at concentrations up to 0.8%. The Panel agreed that the absence of percutaneous absorption, negative oral reproductive and developmental toxicity data, negative oral carcinogenicity data, and negative human skin sensitization data at a concentration of 0.5% preclude any toxicity concerns relating to the use of pentaerythritol tetra-di-t-butyl hydroxyhydrocinnamate as an antioxidant in cosmetic products. The Panel also discussed the issue of incidental inhalation exposure due to the presence of this ingredient in products that are sprayed or those in powder form, but agreed that based on the particle size distribution, small actual exposure in the breathing zone, ingredient use concentrations, and the negative acute oral toxicity data, incidental inhalation would not be a significant route of exposure that might lead to local respiratory or systemic effects.

**Rosmarinus Officinalis (Rosemary)-Derived Ingredients**

The Panel issued a tentative safety assessment with the conclusion that the following eight *rosmarinus officinalis* (rosemary)-derived ingredients are safe as used in cosmetics.

- *rosmarinus officinalis* (rosemary) extract
- *rosmarinus officinalis* (rosemary) flower/leaf/stem extract
- *rosmarinus officinalis* (rosemary) flower/leaf/stem water*
- *rosmarinus officinalis* (rosemary) leaf
- *rosmarinus officinalis* (rosemary) leaf oil
- *rosmarinus officinalis* (rosemary) leaf powder
- *rosmarinus officinalis* (rosemary) leaf water
- *rosmarinus officinalis* (rosemary) water

*Not reported to be in current use. If this ingredient is not in current use were 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 Panel also concluded that *rosmarinus officinalis* (rosemary) leaf extract is safe at ≤0.2% in leave-on products and safe as used in rinse-off products. Although the Panel requested at the September 2013 meeting, dermal sensitization data for *rosmarinus officinalis* (rosemary) leaf extract at the highest reported use concentration (i.e., 10%), the data submitted were on formulations containing ≤0.2% *rosmarinus officinalis* (rosemary) Leaf Extract.

Further, the Panel concluded that the available data are insufficient for determining that *rosmarinus officinalis* (rosemary) flower extract is safe for use in cosmetics because information on the chemical characterization of the flower was not provided.

If the Research Institute of Fragrance Materials (RIFM) confirms that *rosmarinus officinalis* (rosemary) flower/leaf/stem water, *rosmarinus officinalis* (rosemary) leaf water, and *rosmarinus officinalis* (rosemary) water are used as fragrance ingredients only, these ingredients will be deleted from the safety assessment because they will be under the purview of the RIFM, as specified in the CIR Procedures.

The Panel discussed the positive results observed in a reproductive and development toxicity study in rats fed 500 mg/kg/day *rosmarinus officinalis* (rosemary) leaf extract. The Panel noted that these results were attributable to exposures that substantially exceed those that can reasonably be expected through the use of cosmetic products containing these ingredients. The Panel also noted that the caution in the *PDR for Herbal Medicines* that rosemary preparations should not be used during pregnancy refers to the use of rosemary at very high concentrations in drug preparations. The Panel concluded that reproductive and developmental toxicity is not a concern for *Rosmarinus officinalis* (rosemary)-derived ingredients as used in cosmetics.

Additionally, the Panel noted that botanical ingredients are complex mixtures derived from natural plant sources. Because final product formulations may contain multiple botanical ingredients, each containing potentially sensitizing levels of constituents of concern, formulators are advised to be aware of these constituents and to avoid reaching levels that may be hazardous to consumers. Specific examples of constituents of *Rosmarinus officinalis*-derived ingredients that could possibly induce sensitization or other adverse effects are caffeic acid, thujone, and terpenes, especially linalool, linalyl acetate, limonene, and methyleugenol.
Tocopherols

The Panel re-opened the 2002 review of the tocopherols to include the tocotrienols and additional tocopherol ingredients, and issued a tentative amended report with the conclusion that all of these ingredients are safe as used in cosmetics.

In 2002, the Panel concluded that the following nine tocopherols are safe as used in cosmetics:

- tocopherol
- tocopheryl acetate
- tocopheryl linoleate
- tocopheryl linoleate/oleate
- tocopheryl nicotinate
- tocopheryl succinate
- dioleyl tocopheryl methylsilanol
- potassium ascorbyl tocopheryl phosphate
- tocophersolan

At this meeting, the Panel determined that the safety of these tocopherols could be extrapolated to determine the safety of the following five cosmetic ingredients that are included in this safety assessment:

- tocotrienols
- ascorbyl tocopheryl acetate*
- ascorbyl tocopheryl maleate
- tocopheryl phosphate*
- sodium tocopheryl phosphate

*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 current reported maximum use concentrations of tocopherol is higher than what was reported in the original assessment, and that irritation and sensitization data at these higher concentrations are not included in the current report. However, the Panel acknowledged that dermal reactions to tocopherol are rare, and that the North America Contact Dermatitis Group deleted this ingredient from its standard testing because of the rarity of reactions.

The Panel concurred with the Industry’s request that epidemiology studies suggesting that vitamin E supplementation is not always protective against free radical damage, and may be detrimental, be included in the final report. The Panel stated that this information does not affect the safe use conclusion for tocopherols in cosmetics.

Insufficient Data Announcement

Camellia Sinensis-Derived Ingredients

The Panel issued an Insufficient Data Announcement and requested the following additional data to support the safety of Camellia sinensis-derived ingredients:

- Method of manufacture, including removal of impurities and constituents of concern (such as linalool)
- Composition data for camellia sinensis root extract, seedcoat powder, flower extract, and flower/leaf/stem juice
- Concentration of use data for camellia sinensis root extract, seedcoat powder, flower extract, flower/leaf/stem juice, and the catechins
- Human repeated insult patch test (HRIPT) on camellia sinensis leaf (100%), camellia sinensis stem/leaf extract (3%), and camellia sinensis catechins (at use concentrations)
- Confirmation that camellia sinensis leaf water is only used as a fragrance ingredient
- Information on the difference between leaf oil and leaf essential oil

The data listed above are requested to support the safety of 15 ingredients in this report:

- camellia sinensis leaf extract
- camellia sinensis catechins
- camellia sinensis flower extract
- camellia sinensis flower/leaf/stem juice
- camellia sinensis leaf
- camellia sinensis leaf oil
- camellia sinensis leaf powder
- camellia sinensis leaf water
- camellia sinensis root extract
- camellia sinensis seedcoat powder
- camellia sinensis seed extract
- camellia sinensis seed powder
- camellia sinensis seed oil
- hydrolyzed camellia sinensis leaf
- hydrolyzed camellia sinensis seed extract
The *Camellia sinensis* plant is the source of the beverage tea used for human consumption (e.g., white, green, oolong, black). Functions include: antifungal agent; antimicrobial agent; antioxidant; cosmetic astringent; fragrance ingredient; light stabilizer; oral care agent; skin protectant; skin-conditioning agent – emollient; skin-conditioning agent – humectant; and skin-conditioning agent – miscellaneous.

Camellia sinensis leaf extract was reported to be used in 1011 leave-on, 710 rinse-off, and 35 bath cosmetic products up to 3% in leave-on products. Camellia sinensis leaf was reported to be used in 38 leave-on, 14 rinse-off, and 1 bath product, up to 97% in tea bags for the eyes. Camellia sinensis leaf powder was reported to be used in 7 leave-on and 8 rinse-off products, up to 50% in leave-on products. Camellia sinensis leaf water was reported to be used in 26 leave-on and 11 rinse-off products, up to 30% in mascara.

**Re-review and New Data**

**Alpha Hydroxy Acids**

The Panel reaffirmed the 1998 conclusion that glycolic and lactic acid, their common salts and their simple esters are safe for use in cosmetic products at concentrations ≤10%, at final formulation pH ≥3.5, when formulated to avoid increasing sun sensitivity or when directions for use include the daily use of sun protection. These ingredients are safe for use in salon products at concentrations ≤30%, at final formulation pH ≥3.0, in products designed for brief discontinuous use followed by thorough rinsing from the skin, when applied by trained professionals, and when application is accompanied by directions for the daily use of sun protection. The report included the following 22 ingredients:

- glycolic acid
- ammonium glycolate
- calcium glycolate
- potassium glycolate
- sodium glycolate
- methyl glycolate
- ethyl glycolate
- propyl glycolate
- butyl glycolate
- lactic acid
- ammonium lactate
- calcium lactate
- potassium lactate
- sodium lactate
- TEA-lactate
- methyl lactate
- ethyl lactate
- isopropyl lactate
- butyl lactate
- lauryl lactate
- myristyl lactate
- cetyl lactate

The Panel commented that the original report is robust and new data did not indicate that the 1998 report should be re-opened. Although the frequency of use has increased substantially since the original review, the types of use are similar. The Panel noted that the negative results obtained in the NTP mouse photocarcinogenicity study with up to 10% glycolic acid supported the Panel’s original conclusion and current decision to not re-open this safety assessment.

The Panel stated that the re-review summary should clarify the different types and concentrations of use of alpha hydroxy acids that are typical of cosmetic use versus medical use. The Panel requested that industry provide information on the specific types of use categorized as cosmetic use (versus medical use). The Panel also requested that industry clarify the differences between cosmetic use and salon use, and confirm that salon use is considered to be cosmetic use.

Finally, the Panel noted that since the original safety assessment was published by the CIR, the FDA issued a guidance document in 2005 titled, “Guidance for Industry: Labeling for Cosmetics Containing Alpha Hydroxy Acids.” The FDA considered evidence that suggested that use of any topically applied cosmetic products containing alpha hydroxy acids as ingredients may increase the sensitivity of skin to the sun while the products are used, and for up to a week after use is stopped, and that this increased skin sensitivity to the sun may increase the possibility of sunburn.

**Polyvinyl Alcohol**

The Expert Panel reaffirmed the original conclusion that polyvinyl alcohol is safe in the present practices of use and concentration in cosmetics.

Current use data from the FDA indicate that uses have increased from 37 to 225, with a majority of uses in leave-on products. Use concentrations changed from a maximum of 25% with up to 13% hydrolyzed polyvinyl alcohol used in mud packs to current highest maximum concentrations ranging from 0.0035% to 15% in “other” skin care products. The Panel felt that the safety data from the original report, coupled with recognized uses in medical applications, are sufficient to support the increased number of uses.
Sodium α-Olefin Sulfonates

The Panel reaffirmed the original conclusion that sodium α-olefin sulfonates are safe as used in rinse-off products and safe up to 2% in leave-on products.

In the original report, the Panel stated that concentrations of the gamma sultone impurity of final product formulations be limited to: ≤10 ppm unsubstituted alkane sultones; ≤ 1 ppm chlorosultones; and ≤ 0.1 ppm unsaturated sultones. The ingredients in this re-review are:

- sodium C14-16 olefin sulfonate
- sodium C12-14 olefin sulfonate
- sodium C14-18 olefin sulfonate
- sodium C16-18 olefin sulfonate

The use of sodium C14-16 olefin sulfonate has increased from 93 to 300 reported products and is reported to be used at concentrations up to 1.2% in leave-on products and 19% in rinse-off products. Sodium C14-18 olefin sulfonate is reported to be used in 5 rinse-off products and sodium C12-14 olefin sulfonate is reported to be used in rinse-off products up to 5%. There were no reported uses for sodium C16-18 olefin sulfonate. These ingredients function in cosmetics as surfactant – cleansing agents.

The Panel examined toxicity, irritation, and sensitization data that became available since the original safety assessment in 1998. Recent use data reports that the maximum concentration of use for leave-on products has decreased to 1.2% from 10%.

Re-review Summaries

The Panel approved the summary of their action at the September 2013 meeting at which they determined to not reopen the safety assessment of iodopropynyl butylcarbamate.

Reports Tabled

Hydroquinone and p-Hydroxyanisole

The Panel tabled their discussion on hydroquinone and p-hydroxyanisole to allow for the inclusion of new information on the safety of using UV light to cure nail polish gels and for the collection of additional information on the use of UV light to set nail polish gels.

At the March 2013 meeting, the Panel agreed to reopen and to combine these two ingredients because of a new use in an ultraviolet light cured nail polish. Hydroquinone was reaffirmed (in a 2010 report) to be safe at 0.5% when used in a nail adhesive. In 1985, the Panel concluded that p-hydroxyanisole was unsafe because of the data indicating skin depigmentation (in animals) that occurred very close to the level of use that might occur in a cosmetic. CIR has not assessed the use of these ingredients in UV-cured polishes.

Hydroquinone and p-hydroxyanisole (also known as MEHQ or hydroquinone monomethyl ether) are not added to nail products, but are sold with the monomers and oligomers as polymerization inhibiting chemicals. Nail gels that contain hydroquinone and p-hydroxyanisole are reported to be cured or cause polymerization to occur under light in the 390-420 nm range. Recent use data reported that hydroquinone was used in 7 nail extenders and 11 skin care preparations. In a survey conducted by industry, no uses were reported for p-hydroxyanisole and no concentrations of use were reported for either ingredient.

Botanical Guidance and Boiler Plate Language

The CIR Expert Panel approved framework statements and guidelines for reports on botanical ingredients. The approved language emphasizes several considerations likely to be important to the safety assessment of many botanical ingredients, including the presence of heavy metals, pesticides, aflatoxins, and constituents of concern in such ingredients. The Panel emphasized that, because final product formulations may contain multiple botanical ingredients, each containing similar constituents of concern, formulators are advised to be aware of these constituents and to avoid reaching levels that may be hazardous to consumers. The Panel stated that knowledge of the actual levels of constituents of concern in cosmetic ingredients is essential, and that it is industry’s responsibility to characterize such ingredients adequately and to ensure that the total concentrations of constituents of concern do not exceed levels of concern in the final product formulation. The Panel also emphasized that safety assessments should specify the constituents of concern and the attendant adverse health endpoints, as appropriate.
Memorandum

To: CIR Expert Panel Members and Liaisons
From: Lillian Gill, Director, CIR
Date: February 21, 2014
Subject: Re-Review Summaries

At the December 2013 meeting, the Panel determined to not re-open the safety assessment of Alpha Hydroxy Acids, Polyvinyl Alcohol, and Sodium α-Olefin Sulfonates.

The attached re-review summaries are included for your review and approval.
Alpha Hydroxy Acids

CONCLUSION: In 1998, the Expert Panel concluded that glycolic and lactic acid, their common salts and their simple esters, are safe for use in cosmetic products at concentrations ≤10%, at final formulation pH ≥3.5, when formulated to avoid increasing sun sensitivity or when directions for use include the daily use of sun protection. These ingredients are safe for use in salon products at concentrations ≤30%, at final formulation pH ≥3.0, in products designed for brief discontinuous use followed by thorough rinsing from the skin, when applied by trained professionals, and when application is accompanied by directions for the daily use of sun protection. The report included the following 22 ingredients:

<table>
<thead>
<tr>
<th>Glycolic Acid</th>
<th>Lactic acid</th>
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<tbody>
<tr>
<td>Ammonium Glycolate</td>
<td>Ammonium Lactate</td>
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<tr>
<td>Calcium Glycolate</td>
<td>Calcium Lactate</td>
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<td>Sodium Glycolate</td>
<td>Sodium Lactate</td>
</tr>
<tr>
<td>Methyl Glycolate</td>
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<td>Methyl Lactate</td>
</tr>
<tr>
<td>Propyl Glycolate</td>
<td>Ethyl Lactate</td>
</tr>
<tr>
<td>Butyl Glycolate</td>
<td>Isopropyl Lactate</td>
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<td>Myristyl Lactate</td>
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<tr>
<td></td>
<td>Cetyl Lactate</td>
</tr>
</tbody>
</table>

The Expert Panel reviewed newly available studies since that assessment, along with updated frequency and concentration of use information (Table 1). The Expert Panel reaffirmed the original conclusion stated above.

DISCUSSION: The Panel reviewed the data that are newly available for glycolic and lactic acid, their common salts, and their simple esters (referred to as alpha hydroxy acid (AHA) ingredients) since the 1998 safety assessment was published, and reaffirmed the existing conclusion. The Panel noted that the frequency of use of the AHAs has increased considerably since the original assessment. Glycolic acid was used in 42 formulations in 1997, but is currently reported to be used in 337 cosmetic formulations, and lactic acid was reported in 342 formulations in 1997, but is now reported to be used in 1042 formulations. The maximum leave-on use concentrations of glycolic and lactic acids are similar to those reported in the 1998 assessment; however, the highest maximum use concentrations in rinse-off products have increased. The Panel stated that the language crafted in the original conclusion addresses the safe use of AHAs in cosmetic formulations.

The Panel referred to the FDA’s “Guidance for Industry: Labeling for Cosmetics Containing Alpha Hydroxy Acids” that was issued in 2005, which also addressed the use of sun protection with AHA products. The FDA recommended that the labeling of a cosmetic product that contains an AHA as an ingredient and that is topically applied to the skin or mucous membrane bear a statement that conveys the following information:

Sunburn Alert: This product contains an alpha hydroxy acid (AHA) that may increase your skin's sensitivity to the sun and particularly the possibility of sunburn. Use a sunscreen, wear protective clothing, and limit sun exposure while using this product and for a week afterwards.

The statement should appear prominently and conspicuously once in the labeling of a cosmetic product. This guidance does not apply to drug-cosmetic products that contain an AHA as an ingredient and also are labeled to contain a sunscreen for sun protection.

It was reiterated by the Panel that there are three categories of use of AHA ingredients: consumer use, salon use, and medical use. The Expert Panel stressed that this review does not address the medical use of AHA ingredients; this review addresses only the consumer and salon use, i.e., those products available to the general public and those applied by trained estheticians, respectively.

Lastly, the Panel discussed the photocarcinogenicity studies that have been published since the release of the original safety assessment. In these studies, the dermal application of glycolic acid to mouse skin did not increase the incidence of skin tumors in mice. The Panel stated these studies provided additional evidence to confirm the safety of AHAs for use in cosmetic formulations.
<table>
<thead>
<tr>
<th>Exposure Type</th>
<th>Incidental Inhalation-Powder</th>
<th>Incidental Inhalation-Spray</th>
<th>Incidental Ingestion</th>
<th>Dermal Contact</th>
<th>Hair - Non-Coloring</th>
<th>Nail</th>
<th>Mucous Membrane</th>
<th>Baby Products</th>
<th>Sodium Glycolate</th>
<th>Lactic Acid</th>
<th>Calcium Lactate</th>
<th>Ammonium Lactate</th>
</tr>
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<tbody>
<tr>
<td><strong>Duration of Use</strong></td>
<td><strong>Leaves-Off</strong></td>
<td><strong>Rinse-Off</strong></td>
<td><strong>Diluted for (Bath) Use</strong></td>
<td><strong>Incidental Inhalation-Spray</strong></td>
<td></td>
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<td><strong>Baby Products</strong></td>
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**Table 1. Current and historical frequency and concentration of use of AHAs according to duration and exposure**
Table 1. Current and historical frequency and concentration of use of AHAs according to duration and exposure

<table>
<thead>
<tr>
<th>Exposure Type</th>
<th>2013* # of Uses</th>
<th>1997† Max Conc of Use (%)</th>
<th>2013* # of Uses</th>
<th>1997† Max Conc of Use (%)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Potassium Lactate</td>
<td>Sodium Lactate</td>
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<td>Potassium Lactate</td>
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<td><strong>Incidental Inhalation</strong></td>
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<td>14**</td>
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<td>14**</td>
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<tr>
<td><strong>Incidental Inhalation-Spray</strong></td>
<td>14**</td>
<td>14**</td>
<td></td>
<td>14**</td>
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<tr>
<td><strong>Incidental Inhalation-Powder</strong></td>
<td>14**</td>
<td>14**</td>
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</table>

<table>
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<tr>
<th>Duration of Use</th>
<th>2013* # of Uses</th>
<th>1997† Max Conc of Use (%)</th>
<th>2013* # of Uses</th>
<th>1997† Max Conc of Use (%)</th>
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</thead>
<tbody>
<tr>
<td><strong>Leave-On</strong></td>
<td>16</td>
<td>0.0004-0.92 NR</td>
<td>18</td>
<td>0.0002-1.00 NR</td>
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<td><strong>Rinse-Off</strong></td>
<td>11</td>
<td>NR</td>
<td>11</td>
<td>NR</td>
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</table>

<table>
<thead>
<tr>
<th>Duration of Use</th>
<th>2013* # of Uses</th>
<th>1997† Max Conc of Use (%)</th>
<th>2013* # of Uses</th>
<th>1997† Max Conc of Use (%)</th>
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</thead>
<tbody>
<tr>
<td><strong>Leave-On</strong></td>
<td>15</td>
<td>0.06-0.07 (&lt;0.1†)</td>
<td>15</td>
<td>0.06-0.07 (&lt;0.1†)</td>
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<tr>
<td><strong>Rinse-Off</strong></td>
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<td>NR</td>
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<th>Duration of Use</th>
<th>2013* # of Uses</th>
<th>1997† Max Conc of Use (%)</th>
<th>2013* # of Uses</th>
<th>1997† Max Conc of Use (%)</th>
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<tr>
<td><strong>Leave-On</strong></td>
<td>47</td>
<td>0.5-10.2</td>
<td>53</td>
<td>0.5-10.2</td>
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<td>0.015-1.2</td>
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<td>0.015-1.2</td>
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<table>
<thead>
<tr>
<th>Duration of Use</th>
<th>2013* # of Uses</th>
<th>1997† Max Conc of Use (%)</th>
<th>2013* # of Uses</th>
<th>1997† Max Conc of Use (%)</th>
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<td>0.015-1.2</td>
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<td>0.015-1.2</td>
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<table>
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<tr>
<th>Duration of Use</th>
<th>2013* # of Uses</th>
<th>1997† Max Conc of Use (%)</th>
<th>2013* # of Uses</th>
<th>1997† Max Conc of Use (%)</th>
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<td>0.015-1.2</td>
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<td>0.015-1.2</td>
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</table>
Table 1. Current and historical frequency and concentration of use of AHAs according to duration and exposure

<table>
<thead>
<tr>
<th></th>
<th># of Uses</th>
<th>Max Conc of Use (%)</th>
<th></th>
<th># of Uses</th>
<th>Max Conc of Use (%)</th>
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<tbody>
<tr>
<td></td>
<td>Lauryl Lactate</td>
<td>Methyl Lactate</td>
<td>Lauryl Lactate</td>
<td>Methyl Lactate</td>
<td>Lauryl Lactate</td>
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<tr>
<td>Totals*</td>
<td>26</td>
<td>13</td>
<td>0.14-10</td>
<td>0.1-5(^*) ((\leq0.1-1.25)**)</td>
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<td><strong>Duration of Use</strong></td>
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<tr>
<td>Leave-On</td>
<td>209</td>
<td>187</td>
<td>0.01-13.2</td>
<td>&gt;1.5-1(^*) (0.1-50)**</td>
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</tr>
<tr>
<td>Rinse-Off</td>
<td>6</td>
<td>8</td>
<td>0.79-11.2</td>
<td>0.1-1(^*)</td>
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<tr>
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<td>NR</td>
<td>NR</td>
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<tr>
<td>Eye Area</td>
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<td>0.1(^a)</td>
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<tr>
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<td>NR</td>
<td>1</td>
<td>1-25(^c)</td>
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<tr>
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<td>NR</td>
<td>0.14-10(^a)</td>
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<tr>
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<td>NR(^a)</td>
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<td>0.14</td>
<td>(\leq0.1)**</td>
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<tr>
<td>Hair-Coloring</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR(^**)</td>
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<tr>
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<td>NR</td>
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<td>NR(^**)</td>
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<tr>
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<td>1</td>
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<tr>
<td>Baby Products</td>
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<td>&gt;1.5-1(^*) (0.1-50)**</td>
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<td>NR</td>
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<td><strong>Exposure Type</strong></td>
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<td>53</td>
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<td>22(^c)</td>
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<td>NR(^**)</td>
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<td>NR</td>
<td>0.1-1(^*)</td>
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<tr>
<td>Hair-Coloring</td>
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<td>NR</td>
<td>NR(^**)</td>
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<td>Baby Products</td>
<td>NR</td>
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<td>NR</td>
<td>NR(^**)</td>
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Table 2. AHAs not in current use according to VCRP and Council survey data

- Butyl Glycolate
- Calcium Glycolate
- Ethyl Glycolate
- Methyl Glycolate
- Potassium Glycolate
- Propyl Glycolate
- Isopropyl Lactate
REFERENCES


Re-review Summary of Sodium α-Olefin Sulfonates

In a 1998 safety assessment of sodium α-olefin sulfonates, the Cosmetic Ingredient Review (CIR) Expert Panel stated that these ingredients are safe as (then) used in cosmetic products in rinse-off products and safe use was limited to 2% in leave-on products. Concentrations of the gamma sultone impurity of any formulations are limited to: unsubstituted alkane sultones, ≤10 ppm; chlorosultones, ≤ 1 ppm; and unsaturated sultones, ≤ 10 ppm. The Expert Panel reviewed newly available studies since that assessment, along with updated information regarding product types and concentrations of use, and did not reopen this safety assessment. The Panel confirmed that sodium α-olefin sulfonates are safe as cosmetic ingredients in the practices of use and concentration as given in Table 1 with the qualifications mentioned above.

The ingredients in this re-review are:

• Sodium C14-16 Olefin Sulfonate
• Sodium C12-14 Olefin Sulfonate
• Sodium C14-18 Olefin Sulfonate
• Sodium C16-18 Olefin Sulfonate

The new data reviewed by the Panel was collected from the European Chemicals Agency (ECHA) database in the form of robust summaries of studies on sodium C14-16 olefin sulfonate. Data were available on oral toxicity, reproductive and developmental toxicity, genotoxicity, carcinogenicity, irritation, and sensitization.

In 2013, data on ingredient usage are provided to the Food and Drug Administration (FDA) Voluntary Cosmetic Registration Program (VCRP; Table 1). A survey was conducted by the Personal Care Products Council (Council) of the maximum use concentrations for these ingredients in 2013. Sodium C14-16 olefin sulfonate was reported to be used in 11 leave-on products, 247 rinse-off products, and 42 products that are diluted for bath. These include 6 baby products, 36 hair products, 1 lipstick, and 171 personal cleanliness products. Sodium C14-16 olefin sulfonate was reported to be used up to 13.2% in leave-on products, 19% in rinse-off products, and 10% in bath products. This includes use up to 10% in bubble baths and bath soaps and detergents, 19% in shampoos, and 13.2% in other personal cleanliness products. There were no concentrations of use reported for any baby products. Sodium C14-18 olefin sulfonate was reported to be used in 5 shampoos. Sodium C14-18 olefin sulfonate is used up to 16% in shampoos. According to the VCRP, there were no reported uses for sodium C12-14 olefin sulfonate. The Council reported that sodium C12-14 olefin sulfonate is used up to 5% in rinse-off products, including shampoos, hair tints, and skin cleansing preparations. There were no frequencies or concentrations of use reported for sodium C16-18 olefin sulfonate.
Table 1. Current and historical frequency and concentration of use of sodium α-olefin sulfonates according to duration and exposure.1,4-7

<table>
<thead>
<tr>
<th></th>
<th># of Uses</th>
<th>Max Conc of Use (%)</th>
<th># of Uses</th>
<th>Max Conc of Use (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2013</td>
<td>1996</td>
<td>2013</td>
<td>1996</td>
</tr>
<tr>
<td>Sodium C14-16 olefin sulfonate</td>
<td>300</td>
<td>93</td>
<td>0.12-19</td>
<td>5-10</td>
</tr>
<tr>
<td>Sodium C14-18 olefin sulfonate</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td><strong>Duration of Use</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leave-On</td>
<td>9</td>
<td>2</td>
<td>1.2-13.2</td>
<td>10</td>
</tr>
<tr>
<td>Rinse-Off</td>
<td>247</td>
<td>66</td>
<td>0.12-19</td>
<td>NR</td>
</tr>
<tr>
<td>Diluted for (Bath) Use</td>
<td>42</td>
<td>25</td>
<td>2-10</td>
<td>NR</td>
</tr>
<tr>
<td><strong>Exposure Type</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eye Area</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Incidental Ingestion</td>
<td>1</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Incidental Inhalation-Spray</td>
<td>4</td>
<td>NR</td>
<td>NR</td>
<td>0.12-13.3</td>
</tr>
<tr>
<td>Incidental Inhalation-Powder</td>
<td>3</td>
<td>NR</td>
<td>NR</td>
<td>0.12-13.3</td>
</tr>
<tr>
<td>Dermal Contact</td>
<td>260</td>
<td>64</td>
<td>0.12-13.3</td>
<td>10</td>
</tr>
<tr>
<td>Deodorant (underarm)</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Hair - Non-Coloring</td>
<td>35</td>
<td>28</td>
<td>0.8-19</td>
<td>NR</td>
</tr>
<tr>
<td>Hair-Coloring</td>
<td>2</td>
<td>NR</td>
<td>4.5</td>
<td>NR</td>
</tr>
<tr>
<td>Nail</td>
<td>NR</td>
<td>1</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Mucous Membrane</td>
<td>214</td>
<td>50</td>
<td>0.12-13.2</td>
<td>NR</td>
</tr>
<tr>
<td>Baby Products</td>
<td>6</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Sodium C12-14 olefin sulfonate</td>
<td>NR</td>
<td>NR</td>
<td>0.28-5</td>
<td>NR</td>
</tr>
<tr>
<td>Sodium C16-18 olefin sulfonate</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
</tbody>
</table>

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

It is possible these products are sprays, but it is not specified whether the reported uses are sprays.

NR – no reported use

References


5. Personal Care Products Council. 9-3-2013. Concentration of use by FDA Product Category: Sodium Olefin Sulfonates. 2 pages.

Polyvinyl Alcohol

CONCLUSION: In the 1998 safety assessment of polyvinyl alcohol, the Cosmetic Ingredient Review (CIR) Expert Panel concluded that this ingredient was safe as used in cosmetic products.1 The Expert Panel reviewed newly available studies since that assessment, along with updated frequency and concentration of use information.2-12 The Expert Panel reaffirmed the original conclusion that polyvinyl alcohol is safe as a cosmetic ingredient in the practices of use and concentration as given in Table 1.

DISCUSSION: Newly available data did not raise any issues regarding the safety of polyvinyl alcohol. Polyvinyl alcohol functions as a binder, film former, and viscosity increasing agent in cosmetic products.2 The majority of the uses of polyvinyl alcohol are in eye makeup and skin care products.3 Reported use has increased from 37 uses in 1998 to 225 uses in 2013. The maximum use concentration in 1998 was reported to be ≤ 25.1 A survey of use concentrations conducted by the Personal Care Products Council in 2013 reported maximum concentration of use ranges of 0.0035% to 15%.

<table>
<thead>
<tr>
<th>Table 1. Historical and current use and concentration of use data for polyvinyl alcohol,1,3,4</th>
</tr>
</thead>
<tbody>
<tr>
<td># of Uses</td>
</tr>
<tr>
<td>Polyvinyl Alcohol</td>
</tr>
<tr>
<td>Data Year</td>
</tr>
<tr>
<td>Totals</td>
</tr>
<tr>
<td>Duration of Use</td>
</tr>
<tr>
<td>Leave-On</td>
</tr>
<tr>
<td>Rinse-Off</td>
</tr>
<tr>
<td>Diluted for (Bath) Use</td>
</tr>
<tr>
<td>Exposure Type</td>
</tr>
<tr>
<td>Eye Area</td>
</tr>
<tr>
<td>Incidental Ingestion</td>
</tr>
<tr>
<td>Incidental Inhalation-Spray?2,5</td>
</tr>
<tr>
<td>Confirmed Spray</td>
</tr>
<tr>
<td>Incidental Inhalation-Powder?4,5</td>
</tr>
<tr>
<td>Confirmed Powder</td>
</tr>
<tr>
<td>Dermal Contact</td>
</tr>
<tr>
<td>Deodorant (underarm)-Spray?2</td>
</tr>
<tr>
<td>Confirmed Spray</td>
</tr>
<tr>
<td>Not Spray</td>
</tr>
<tr>
<td>Hair - Non-Coloring</td>
</tr>
<tr>
<td>Hair-Coloring</td>
</tr>
<tr>
<td>Nail</td>
</tr>
<tr>
<td>Mucous Membrane</td>
</tr>
<tr>
<td>Baby Products</td>
</tr>
<tr>
<td>NR = Not reported</td>
</tr>
<tr>
<td>2.</td>
</tr>
<tr>
<td>3.</td>
</tr>
<tr>
<td>4.</td>
</tr>
<tr>
<td>5.</td>
</tr>
</tbody>
</table>

a Use concentrations not well detailed in 1998, a general maximum use concentration was reported to be ≤ 25% for all product uses. Specific use concentration data were provided for a few specific product categories.


4. Personal Care Products Council. 9-3-2013. Concentration of Use by FDA Product Category: Polyvinyl Alcohol. 2 pages.


12. McDonald CC, Kaye SB, Figueiredo FC, Macintosh G, and Lockett C. A randomised, crossover, multicentre study to compare the performance of 0.1% (w/v) sodium hyaluronate with 1.4% (w/v) polyvinyl alcohol in the alleviation of symptoms associated with dry eye syndrome. *Eye*. 2002;16:601-607.