Cosmetic Ingredient Review Expert Panel
129th Meeting (December 9, 2013) - Findings

December 13, 2013

• Final Safety Assessments
  • *Achillea millefolium* (Yarrow)-Derived Ingredients – 3 ingredients
  • Alumina and Aluminum Hydroxide – 2 ingredients
  • Amino Acid Alkyl Amides – 115 ingredients
  • *Anthemis nobilis*-Derived Ingredients – 4 ingredients
  • *Chamomilla recutita*-Derived Ingredients – 11 ingredients
  • Formic Acid and Sodium Formate – 2 ingredients
  • Phytosterols – 26 ingredients

• Tentative Safety Assessments
  • Alkyl Betaines – 11 ingredients
  • Monosaccharides, Disaccharides, and Related Ingredients – 25 ingredients
  • Pentaerythrityl Tetra-Di-t-Butyl Hydroxyhydrocinnamate – 1 ingredient
  • *Rosmarinus officinalis* (Rosemary)-Derived Ingredients – 10 ingredients
  • Tocopherol and Tocotrienols – 14 ingredients

• Insufficient Data Announcements
  • Camellia Sinensis Leaf Ingredients – 14 ingredients

• Re-review and re-review summaries
  • Alpha-Hydroxy Acids – not reopened
  • Polyvinyl Alcohol – not reopened
  • Sodium α-Olefin Sulfonates – not reopened
  • Re-review summary for Iodopropynyl Butylcarbamate – approved

• 129th Meeting Notes
  • Director’s report
  • Report tabled
    □ Hydroquinone & p-Hydroxyanisole – 2 ingredients
  • Botanical Guidance and Boilerplate
  • Scientific literature reviews posted on the CIR website
  • Re-reviews for the next Panel meeting
  • Scientific Literature Reviews under development
  • Next CIR Expert Panel Meeting – Monday and Tuesday, March 17-18, 2014
Final Safety Assessments

Any interested person who believes that a final safety assessment or final amended safety assessment is incorrect may petition the CIR Expert Panel to amend the safety assessment. Unpublished data cited as references in CIR safety assessments are available for review. Final safety assessments and final amended safety assessments will be posted on the CIR website at www.cir-safety.org.

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 glycine
- 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
- dipalmitoyl cysteine*
- dipotassium capryloyl glutamate
- dipotassium undecylencyoyl glutamate*
- disodium caproyl glutamate
- disodium cocooyl glutamate
- disodium hydrogenated tallow glutamate
- disodium N-lauroyl aspartate*
- disodium lauroyl glutamate
- disodium malyl tyrosinate
- disodium stearoyl glutamate
- disodium undecylencyoyl 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 glycerine  
palmitoyl gold of pleasure amino acids*  
palmitoyl isoleucine*  
palmitoyl keratin amino acids  
palmitoyl oat amino acids*  
palmitoyl pea amino acids*  
palmitoyl proline  
palmitoyl quinoa amino acids*  
palmitoyl silk amino acids  
potassium caproyl tyrosine*  
potassium caproyl glutamate*  
potassium cocoyl glutamate*  
potassium cocoyl glycinate  
**potassium cocoyl/hydrogenated tallow glutamate*  
potassium cocoyl oat amino acids*  
potassium cocoyl palmoyl/sunfloweroyl glutamate*  
potassium cocoyl proline*  
potassium cocoyl threoninate*  
potassium cocoyl wheat amino acids*  
potassium lauroyl aspartate  
potassium lauroyl keratin amino acids*  
potassium lauroyl milk amino acids*  
potassium lauroyl oat amino acids  
potassium lauroyl silk amino acids*  
potassium lauroyl wheat amino acids  
potassium myristoyl glutamate  
potassium palmitoyl proline  
potassium whey amino acids*  
potassium whey amino acids*  
potassium whey amino acids*  
potassium whey amino acids*  
potassium whey amino acids*  
propionyl collagen amino acids  
sodium caproyl prolinate*  
sodium caproyl glutamate*  
sodium cocoyl alaninate  
sodium cocoyl amino acids  
sodium cocoyl barley amino acids*  
sodium cocoyl collagen amino acids  
sodium cocoyl glutamate  
sodium cocoyl glutaminate*  
sodium cocoyl glycinate  
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 milk amino acids*  
sodium lauroyl oat amino acids  
sodium lauroyl sunfloweroyl glutamate*  
sodium lauroyl wheat amino acids  
sodium lauroyl/myristoyl aspartate*  
sodium lauroyl/wheat amino acids  
sodium lauroyl/TEA-lauroyl collagen amino acids*  
sodium lauroyl/TEA-lauroyl keratin amino acids*  
sodium lauroyl/TEA-undecylenoyl collagen amino acids*  
sodium undecylenoyl glutamate*  
stearyl glutamic acid*  
stearyl glutamate  
stearyl leucine*  
TEA-cocoyl alaninate  
TEA-cocoyl glutamate  
TEA-cocoyl glutaminate*  
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 water |
| Chamomilla recutita (matricaria) flower extract | Chamomilla recutita (matricaria) flower oil |
| Chamomilla recutita (matricaria) flower powder | |

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/stem water |
| Chamomilla recutita (matricaria) flower/leaf extract | Chamomilla recutita (matricaria) leaf water |
| Chamomilla recutita (matricaria) flower/leaf/stem extract | Chamomilla recutita (matricaria) oil |

The Panel reviewed new skin irritation and sensitization data on facial cleansing and makeup remover towelettes containing 0.00006% 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 | phytosteryl isostearate |
| Canola sterols* | phytosteryl linoleate* |
| C10-40 isoalkyl acid phytosterol esters* | phytosteryl linoleate/linolenate* |
| Dihydrophytosterol octyldodecanoate* | phytosteryl macadamiate |
| Euterepe oleracea sterols | phytosteryl nonanoate* |
| Glycine soja (soybean) sterols | phytosteryl oleate |
| Persea gratissima (avocado) sterols | phytosteryl rice branate |
| Phytosterols | phytosteryl ricinoleate* |
| Phytosteryl butyrate* | phytosteryl sunflowerseedate* |
| Phytosteryl canolate | Punica granatum sterols* |
| Phytosteryl caprylate/caprate* | Beta-sitosterol |
| Phytosteryl hydroxystearate* | Beta-sitosterol acetate* |
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**

These tentative safety assessments will be posted on the CIR website at [www.cir-safety.org](http://www.cir-safety.org) on or before December 20, 2013. Interested persons are given 60 days to comment, provide information and/or request an oral hearing before the CIR Expert Panel. Information may be submitted without identifying the source or the trade name of the cosmetic product containing the ingredient. All unpublished data submitted to CIR will be discussed in open meetings, and are available for review by any interested party. Please submit data and/or comments to CIR by February 14, 2014, or sooner if possible. These reports may be scheduled for review by the CIR Expert Panel at its March 17-18, 2014 meeting.

**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.

<table>
<thead>
<tr>
<th>Betaine</th>
<th>Betaine</th>
</tr>
</thead>
<tbody>
<tr>
<td>betaine</td>
<td>myristyl betaine</td>
</tr>
<tr>
<td>behenyl betaine</td>
<td>oleyl betaine</td>
</tr>
<tr>
<td>cetyl betaine</td>
<td>stearyl betaine</td>
</tr>
<tr>
<td>coco-betaine</td>
<td>tallow betaine*</td>
</tr>
<tr>
<td>decyl betaine*</td>
<td>hydrogenated tallow betaine*</td>
</tr>
<tr>
<td>lauryl betaine</td>
<td></td>
</tr>
</tbody>
</table>

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

The Panel considered the available data 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:

<table>
<thead>
<tr>
<th>Monosaccharide</th>
<th>Monosaccharide</th>
</tr>
</thead>
<tbody>
<tr>
<td>calcium gluconate</td>
<td>maltose</td>
</tr>
<tr>
<td>fructose</td>
<td>mannose</td>
</tr>
<tr>
<td>fucose*</td>
<td>melibiose</td>
</tr>
<tr>
<td>galactose*</td>
<td>potassium gluconate</td>
</tr>
<tr>
<td>galactosyl fructose*</td>
<td>ribose</td>
</tr>
<tr>
<td>galacturonic acid*</td>
<td>sodium gluconate</td>
</tr>
<tr>
<td>gluconic acid</td>
<td>sucralose</td>
</tr>
<tr>
<td>glucose</td>
<td>sucrose</td>
</tr>
<tr>
<td>isomalt</td>
<td>trehalose</td>
</tr>
<tr>
<td>kefran</td>
<td>xylobiose</td>
</tr>
<tr>
<td>lactitol</td>
<td>xylose</td>
</tr>
<tr>
<td>lactose</td>
<td></td>
</tr>
<tr>
<td>lactulose*</td>
<td></td>
</tr>
</tbody>
</table>
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 Cosmetic”.

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 methylcyclohexen.

**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 tocopherol 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 Announcements**

*For this insufficient data announcement, interested persons are given an opportunity to comment, provide information and/or request an oral hearing before the CIR Expert Panel. Information may be submitted without identifying the source or the trade name of the cosmetic product containing the ingredient. All unpublished data submitted to CIR will be discussed in open meetings, and are available for review by any interested party. Please submit data and/or comments to CIR by February 14, 2014, or sooner if possible. These reports are scheduled for review by the CIR Expert Panel at its March 17-18, 2014 meeting.*

**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 (HRRIPT) 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 root extract
- camellia sinensis seedcoat 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 sulfone impurity of final product formulations be limited to: ≤10 ppm unsubstituted alkane sulfones; ≤1 ppm chlorosulfones; and ≤0.1 ppm unsaturated sulfones. 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.

---

### 129th Meeting Notes

#### 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.

#### 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.

#### Scientific Literature Reviews

- These literature reviews are currently posted on the CIR website at [http://www.cir-safety.org/ingredients/glossary/all](http://www.cir-safety.org/ingredients/glossary/all)
  - alkoxy polysiloxanes
  - PEG-150 pentaerythritol tetrastearate
  - citrus-derived ingredients
Draft reports for these ingredient families, along with any unpublished data submitted by interested parties, may be presented to the Panel at its meeting on March 17-18, 2014.

- These literature reviews are currently in preparation
  - Polyene group
  - Ceramides
  - 2-Amino-3-Hydroxypyridine
  - Avena Sativa (Oat)-derived ingredients
  - Potassium Alkyl Phosphates
  - Plant Polysaccharide Gums
  - Styrene and Vinyl-type Styrene Copolymers

Re-reviews for the next Panel meeting

No re-reviews are scheduled for discussion at the March meeting.

CIR also plans to present the proposed 2015 priority list at the March meeting.

Next CIR Expert Panel Meeting
Monday and Tuesday, March 17-18, 2014 at the Washington Court Hotel, 525 New Jersey Avenue, NW, Washington, DC 20001 --- Please contact Carla Jackson (jacksonc@cir-safety.org) at CIR before the meeting if you plan to attend.