Announcement

Cosmetic Ingredient Review Expert Panel
128th Meeting (September 9-10, 2013) - Findings

September 13, 2013

● Final Safety Assessments
  - Alkyl PEG/PPG Ethers – 131 ingredients
  - Dialkyl Sulfo Succinate Salts – 8 ingredients
  - Hydroxypropyl bis(N-Hydroxyethyl-p-Phenylenediamine) HCl – 1 ingredient
  - Isethionate Salts – 12 ingredients
  - Methyl Glucose Polyethers and Esters – 25 ingredients
  - Polyquaternium-22 and Polyquaternium-39 – 2 ingredients
  - Tromethamine, Aminomethyl Propanediol, and Aminoethyl Propanediol – 3 ingredients

● Tentative Safety Assessments
  - Achillea millefolium (Yarrow)-Derived Ingredients – 3 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
  - Hydrolyzed Wheat Protein and Hydrolyzed Wheat Gluten – 2 ingredients
  - Phytosterols – 26 ingredients

● Insufficient Data Announcements
  - Alkyl Betaines – 11 ingredients
  - Rosmarinus officinalis (Rosemary)-Derived Ingredients – 10 ingredients

● Re-review and re-review summaries
  - Iodopropynyl Butylcarbamate – not reopened
  - Re-review summaries for PVP and Retinol and Retinyl Palmitate – approved

● 128th Meeting Notes
  - Director's report
  - Report tabled
    - Alumina and Aluminum Hydroxide – 2 ingredients
  - 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, December 9-10, 2013
## 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 Unpublished data cited as references in CIR safety assessments are available for review.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](http://www.cir-safety.org).

## Alkyl PEG/PPG Ethers

The Panel issued a final safety assessment with the conclusion that the 131 alkyl PEG/PPG ethers listed below are safe in the present practices of use and concentration in cosmetics when formulated to be non-irritating.

### Alkyl PEG/PPG Ethers

<table>
<thead>
<tr>
<th>Alkyl PEG/PPG Ether</th>
<th>Alkyl PEG/PPG Ether</th>
<th>Alkyl PEG/PPG Ether</th>
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<td>Alkyl PEG/PPG Ether</td>
<td>Alkyl PEG/PPG Ether</td>
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<tr>
<td>PEG-4-PPG-7 C13/C15 Alcohol*</td>
<td>PPG-2 C9-11 Pareth-11*</td>
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<tr>
<td>PEG-2 C9-11 Pareth-7*</td>
<td>PPG-1-Isodeceth-7*</td>
<td>Propylene Glycol Oleth-5*</td>
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</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 maximum reported leave-on use concentrations are up to 10% PEG-5-ceteth-20 in “other” fragrance preparations and in tonics, dressings, and other hair grooming aids, and up to 7% PEG/PPG-14/7 dimethyl ether in face and neck, and body and hand products.

Most of the alkyl PEG/PPG ethers included in this review were reported to function in cosmetics as surfactants, skin conditioning agents, and/or emulsifying agents. The alkyl PEG/PPG ethers share very similar physicochemical properties with another group of ingredients that has been reviewed previously by the CIR Panel and found safe when formulated to be non-irritating, i.e., the alkyl PEG ethers. The only difference between these two families is the inclusion of PPG repeat units, which are used to fine-tune the surfactant properties of this group. The Panel relied on analogous ingredient data, extracted from the alkyl PEG ethers and PPG reports, when making its determination of safety.
Dialky Sulfosuccinate Salts

The Panel issued a final amended safety assessment with the conclusion that the eight dialky sulfosuccinate salts listed below are safe in the present practices of use and concentration in cosmetics when formulated to be non-irritating. Of this grouping, diethylhexyl sodium sulfosuccinate is the only dialky sulfosuccinate salt reported in use. The maximum use concentration is 4.4% in eyebrow pencil formulations.

- ammonium dinonyl sulfosuccinate*
- diamylyl sodium sulfosuccinate*
- diacryl sodium sulfosuccinate*
- diethylhexyl sodium sulfosuccinate
- diheptyl sodium sulfosuccinate*
- disobutyl sodium sulfosuccinate*
- ditridecyl sodium sulfosuccinate*
- diisobutyl sodium sulfosuccinate*
- dihexyl sodium sulfosuccinate*
- diheptyl sodium sulfosuccinate*
- ditridecyl sodium sulfosuccinate*

*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.

In 1998, the Panel revised the original 1994 conclusion of safe at a concentration limit of 0.42%. The Panel amended the 1994 report to conclude that this ingredient is safe as used in cosmetic formulations, stressing that care should be taken to avoid irritancy, especially in those products intended for prolonged contact with the skin.

The Panel reviewed the available animal and clinical data on the dialky sodium sulfosuccinate to determine the safety of this group of ingredients. Although data on the other dialky sulfosuccinate salts were not available, the Panel stated that diethylhexyl sodium sulfosuccinate was a reasonable representative of all of the diesters because they are similar in alkyl chain length, are symmetrically substituted, and have similar functions in cosmetic formulations. Therefore, the Panel found it appropriate to extrapolate the data on diethylhexyl sodium sulfosuccinate to assess the safety of the entire group.

Hydroxypropyl bis(N-hydroxyethyl-p-phenylenediamine) HCl

The Panel issued a final safety assessment with the conclusion that this hair dye ingredient is safe in the present practices of use and concentration.

Hydroxypropyl bis(N-hydroxyethyl-p-phenylenediamine) HCl was reported by the VCRP to be used in 75 hair dyes and colors. In a survey conducted by the Council, the maximum reported use concentration is up to 0.28%. Extensive data developed to support the safe use of this oxidative hair dye ingredient in Europe were reviewed by the Panel. The Panel noted that UV absorption was seen in the UVC region of the spectrum, but because UVC is not present in sunlight, no photochemical interaction was expected during routine use. There was a small absorption peak in the UVB range, but the available phototoxicity data demonstrated no adverse reactions.

The Panel recognized that this coal tar hair dye is exempt from certain adulteration and color additive provisions of the Federal Food, Drug, and Cosmetic Act, when the product label bears a caution statement and patch test instructions for determining whether the product causes skin irritation. Although concerns about such self-testing were considered, the Panel agreed that following this procedure enables consumers to determine, prospectively, whether they will have an irritation/sensitization reaction, and allow them to avoid subsequent significant exposures. In the future, the Panel will consider the results of ongoing studies by the industry to evaluate the risks and benefits of consumer self-testing.

While the safety of individual hair dye ingredients are not addressed in epidemiology studies that seek to determine links, if any, between hair dye use and disease, such studies do provide broad information. Currently available epidemiology studies provide insufficient evidence to support a causal association between personal hair dye use and a variety of tumors and cancers. A detailed summary of the available hair dye epidemiology data is available at http://www.cir-safety.org/cir-findings.

Isethionate Salts

The Panel issued a final amended safety assessment of isethionate salts with the conclusion that the 12 ingredients listed below are safe in the present practices of use and concentration in cosmetics when formulated to be non-irritating.

- sodium cocoyl isethionate
- ammonium cocoyl isethionate
- sodium hydrogenated cocoyl methyl isethionate*
- sodium isethionate
- sodium lauroyl isethionate
- sodium lauroyl methyl isethionate
- sodium methyl isethionate
- sodium myristoyl isethionate*
- sodium oleyl isethionate*
- sodium oleoyl isethionate*
- sodium palm kerneloyl isethionate*
- sodium stearoyl methyl isethionate*

*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.

These ingredients are related by a common 2-hydroxyethanesulfonic acid structural core which has an alcohol moiety and a sulfonic acid at opposing ends of a two carbon alkyl chain. The isethionate salts are reported to function in cosmetics as surfactants. Although there are data gaps in this report, the similarity in chemical structures, physicochemical properties, and functions and concentrations of use in cosmetics allow for grouping these ingredients and interpolating the available toxicological data to support the safety of the entire group. For example, the Panel noted the absence of carcinogenicity data, but considered the data demonstrating that sodium cocoyl isethionate and sodium isethionate were not mutagenic or clastogenic in in vitro genotoxicity studies adequate to support the safety of the entire group.

The potential for irritancy is associated with most surfactants so the data were examined for changes in the pattern and concentration of use since the original safety assessment of sodium cocoyl isethionate. The Panel noted that the concentration of use of sodium cocoyl isethionate in rinse-off products at 53% is essentially the level previously considered safe.

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Methyl Glucose Polyethers and Esters
The Panel issued a final safety assessment with the conclusion that the 25 methyl glucose polyethers and esters listed below are safe in the present practices of use and concentration in cosmetics.

<table>
<thead>
<tr>
<th>Esters:</th>
<th>Polyethers:</th>
<th>Esters and polyethers:</th>
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</thead>
<tbody>
<tr>
<td>methyl glucose caprylate/caprate*</td>
<td>PPG-10 methyl glucose ether</td>
<td>PEG-120 methyl glucose dioleate</td>
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<td>methyl glucose dioleate</td>
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<td>methyl glucose isostearate*</td>
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*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 polyether forms of these ingredients function as skin and hair conditioning agents, whereas, the methyl glucose esters and the ester/polyether forms function only as skin conditioning agents in cosmetic products.

The Panel confirmed their previous conclusion that the toxicity data on isostearic acid, esters with methyl α-D-glucoside support the safe use of methyl glucose sesquistearate, PEG-20 methyl glucose sesquistearate, and PEG-20 methyl glucose distearate in lipsticks. Although data on use concentrations were not available for the use of PEG-20 methyl glucose sesquistearate in lipsticks, the Panel agreed that this ingredient is likely being used at a concentration no greater than the 1% maximum reported for methyl glucose sesquistearate.

Polyquaternium-22 and Polyquaternium-39
The CIR Expert Panel issued a final report with the conclusion that polyquaternium-22 and polyquaternium-39 are safe in the present practices of use and concentration in cosmetics.

Both ingredients function as antistatic agents, film formers, and hair fixatives in cosmetic products, and polyquaternium-22 and polyquaternium-39 are used at concentrations up to 2% and 3%, respectively. Concerns about the potential for residual monomers in cosmetic formulations were addressed in the data submitted for polyquaternium-22 and polyquaternium-39, which showed that the unreacted monomers content was below the levels of toxicological concern. For example, the acrylamide monomer used to manufacture polyquaternium-39 was below the 1 ppm level of detection.

While there is a notable lack of some toxicity data, these are large, highly polar molecules that are not expected to penetrate the skin. The Panel agreement that there is minimal concern about the irritation and sensitization potential is supported by the negative skin irritation and skin sensitization data.

Tromethamine, Aminomethyl Propanediol, and Aminoethyl Propanediol
The CIR Expert Panel issued a final safety assessment with the conclusion that tromethamine, aminomethyl propanediol (AMPD), and aminomethyl propanediol (AEPD) are safe in the present practices of use and concentration in cosmetics.

These ingredients are aliphatic or substituted aliphatic compounds that function as fragrance ingredients and pH adjusters in cosmetics. Tromethamine was reported by the VCRP to be used in 488 leave-on products and 70 rinse-off products, and according to a Council survey, at maximum use concentrations up to 3.7. AMPD was reported by the VCRP to be used in 131 leave-on products and 2 rinse-off products; according to a Council survey the maximum reported use concentration is up to 2% in leave-on products. AEPD is not in use; however, any use in the future is expected to be in product categories and at concentrations comparable to others in this group.

Data submitted to the CIR indicated that the presence of secondary amines and nitrosamines were below the limit of detection of 0.5% weight (maximum) and 50 ppb, respectively. However, because of the possible presence of these compounds, the Panel cautioned that ingredients should not be used in cosmetic products in which N-nitroso compounds can be formed.
Tentative Safety Assessments

These tentative safety assessments will be posted on the CIR website at www.cir-safety.org on or before September 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 November 21, 2013, or sooner if possible. These reports may be scheduled for review by the CIR Expert Panel at its December 9-10, 2013 meeting.

Achillea millefolium-derived ingredients

The Panel issued a tentative amended final report for public comment for the Achillea millefolium-derived ingredients below, with the conclusion that they are safe in the present practices of use and concentration when formulated to be non-sensitizing. This change amends the previous conclusion of safe without qualifications.

- 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 by the VCRP to be used in 135 cosmetic products; according to a Council survey, the maximum reported use concentration is up to 0.04% in leave-on products and up to 0.03% in rinse-off products.

The Panel expressed continued concern that multiple botanical ingredients may each contribute to the final concentration of a single component. Therefore, when formulating products, manufacturers should avoid reaching levels of plant constituents (e.g., hydroquinone, linalool) that may cause sensitization or other adverse effects. The Panel also reiterated that all botanical ingredients potentially 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.

Amino Acid Alkyl Amides

The Panel issued a tentative safety assessment of amino acid alkyl amides with the conclusion that the 115 ingredients 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
- caproyl collagen amino acids
- caproyl glycine
- caproyl gold of pleasure amino acids
- caproyl keratin amino acids
- caproyl pea amino acids
- caproyl quinoa amino acids
- caproyl silk amino acids
- cocoyl glutamic acid
- dipalmitoyl cysteine
- dipotassium caproyl glutamate
- dipotassium undecylenoyl glutamate
- disodium caproyl glutamate
- disodium cocoyl glutamate
- disodium hydrogenated tallow glutamate
- disodium N-lauroyl aspartate
- disodium lauroyl glutamate
- disodium malyl tyrosinate
- disodium stearyl 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
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- potassium caproyl glutamate
- potassium cocoyl glutamate
- potassium cocoyl glycinate
- potassium cocoyl 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 olivoyl/lauroyl wheat amino acids
- potassium stearoyl glutamate
- potassium undecylenoyl glutamate
- propionyl collagen amino acids
- sodium caproyl prolinate
- sodium caproyl glutamate
sodium cocoyl alaninate
sodium cocoyl amino acids
sodium cocoyl apple amino acids
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sodium cocoyl collagen amino acids
sodium cocoyl glutamate
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sodium cocoyl/olivoyl 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 olivoyl glutamate*
sodium palmitoyl proline
sodium palmoyl glutamate
sodium stearoyl glutamate
sodium/TEA-lauroyl collagen amino acids*
sodium/TEA-lauroyl keratin amino acids*
sodium undecylenoyl glutamate* stearoyl glutamic acid*
stearoyl leucine*
TEA-cocoyl alaninate
TEA-cocoyl glutamate
TEA-cocoyl glutaminic acid
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 reviewed additional dermal irritation and sensitization data on lauroyl lysine and sodium lauroyl glutamate at the highest use concentrations reported (45% and 40%, respectively). While these data support the safety of these ingredients under present practices of use and concentration, the Panel emphasized their function as skin and hair conditioning agents and surfactants, and concluded that they should be formulated to be non-irritating.

In the absence of data that clarify 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 with levels of free diethanolamine (DEA) that could be present as an impurity in the ingredients containing triethanolamine (TEA), and stated that the levels of free DEA must not exceed those considered safe by the Panel, as stated in the current report on DEA, which is up to 0.64%. 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 tentative safety assessment with the conclusion that anthemis nobilis flower extract, anthemis nobilis flower oil, anthemis nobilis flower powder, and anthemis nobilis flower water are safe in the present practices of use and concentration in cosmetics when formulated to be non-sensitizing.

In a previous review, the Panel determined that the following additional data were needed to make a determination of safety: (1) composition data on all anthemis nobilis-derived ingredients, except anthemis nobilis flower oil, and (2) skin irritation and sensitization data on all anthemis nobilis ingredients, except anthemis nobilis flower oil, at a use concentration of 10%.

The Panel reviewed HRIPT data on a leave-on product containing 3% anthemis nobilis flower extract. The industry indicated that, according to survey data, the reported use concentration at 10% is for a single skin cleansing product was not representative of the typical use concentration. After considering this information, the Panel determined that the HRIPT data and the available skin irritation and sensitization data are sufficient for evaluating the irritation and sensitization potential of anthemis nobilis-derived ingredients over the range of reported use concentrations. The data provided on the composition of anthemis nobilis flower oil enabled reasonable assumptions about the composition of the remaining anthemis nobilis-derived ingredients.

The Panel expressed concern that multiple botanical ingredients may each contribute to the final concentration of a single component. Therefore, when formulating products, manufacturers should avoid reaching levels of plant constituents that may cause sensitization or other adverse effects. 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.

**Chamomilla recutita-Derived Ingredients**

The Panel issued a tentative report with the conclusion that chamomilla recutita (matricaria) flower, chamomilla recutita (matricaria) flower powder, chamomilla recutita (matricaria) flower water, and chamomilla recutita (matricaria) flower oil are safe in the present practices of use and concentration in cosmetics when formulated to be non-sensitizing.

The Panel also concluded that the available data are insufficient for determining that 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, and chamomilla recutita (matricaria) oil are safe for use in cosmetics.
Chamomilla recutita (matricaria) flower-derived ingredients are used at concentrations up to 0.5%. Negative results submitted in three HRIPT studies for chamomilla recutita (matricaria) flower extract at 0.4% use concentration, and other skin sensitization data, were considered sufficient for evaluating the safety of all flower-derived ingredients. The Panel stated that there were no differences between the flower-derived ingredients and ingredients derived from the whole plant, stem, or leaf. In the absence of chemical characterization data for the whole plant, stem or leaf, the available data are insufficient for evaluating the safety of these ingredients.

The Panel expressed concern that multiple botanical ingredients may each contribute to the final concentration of a single component. Therefore, when formulating products, manufacturers should avoid reaching levels of plant constituents (such as linalool, linalool acetate, farnesene, azulene, terpenes, and terpenoids) that may cause sensitization or other adverse effects. The Panel noted that, in formulations, these constituents should not exceed any limitations that may have been established by the International Fragrance Association (IFRA). 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 formulation.

Formic Acid and Sodium Formate

The Panel issued a tentative 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. At that time the only reported function of formic acid in cosmetics was that of a pH adjuster. In 2012, the Panel reopened the final safety assessment on formic acid to address any safety concerns that may be associated with the new functions as a preservative and to add sodium formate.

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, by far, 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.

Hydrolyzed Wheat Gluten and Hydrolyzed Wheat Protein

The Panel issued a tentative safety assessment of hydrolyzed wheat gluten and hydrolyzed wheat protein with the conclusion 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 into contact with mucous membranes or may be incidentally inhaled.

The Panel felt the data on the elicitation of Type I hypersensitivity reaction in sensitized individuals were adequate to support the safety of hydrolyzed wheat gluten and hydrolyzed wheat protein ingredients with peptide length distributions that do not exceed 30 amino acids. However, no data were available to determine a peptide-length threshold below which sensitization would not be induced in people who are not already sensitized to hydrolyzed wheat gluten or hydrolyzed wheat protein. The Panel noted that a study of mice with tape-striped skin demonstrated the induction of sensitization to hydrolyzed wheat protein with a size distribution ranging from about 40 kDa to 50 kDa (or approximately 360-450 amino acids in length). The Panel also noted reports indicating that people using cosmetic products containing hydrolyzed wheat proteins applied to the eye area were sensitized. Unless data can be produced that demonstrate a size-distribution threshold below which sensitization cannot be induced, cosmetics containing hydrolyzed wheat gluten and hydrolyzed wheat protein should not be used on damaged skin or on mucous membranes. These ingredients should also not be used in products that may be inhaled, like aerosolized sprays.

The Panel asked that the cosmetics industry continue to provide additional data on manufacturing practices, characterization methods, and composition, including peptide size distributions, to enable better characterization of the nature and variability of these ingredients as used in cosmetic products and to enable the Panel to refine its conclusion.

Phytosterols

The Panel issued a tentative safety assessment with the conclusion that the 26 phytosterols listed below were safe as cosmetic ingredients in the present practices of use and concentration. Diosgenin was originally included in this safety assessment, but was removed from the report because it has different characteristics than the rest of the group.

- 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
- phytosterol butyrate
- phytosterol canolate
- phytosterol caprylate/caprate
- phytosterol hydroxystearate
- phytosteryl caprate
- phytosteryl caprylate/caprate
- phytosteryl linoleate
- phytosteryl linoleate/linolenate
- phytosteryl macadamiate
- phytosteryl nonanoate
- phytosteryl oleate
- phytosteryl olate
- phytosteryl palmitate
- phytosteryl ricinoleate
- phytosteryl sunflowerseedate
- punica granatum sterols
- beta-sitosterol
- beta-sitosteryl acetate
Phytosterols occur naturally as free alcohols and fatty acid esters. They exist naturally in plant-based food and are consumed regularly in the diet.

These ingredients function as skin-conditioning agents, hair conditioning agents, viscosity increasing agents, skin protectants, antioxidants, and fragrances. They are used in almost all use categories at concentrations up to 8%.

**Insufficient Data Announcements**

For these insufficient data announcements, 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 November 10, 2013, or sooner if possible. These reports are scheduled for review by the CIR Expert Panel at its December 9-10, 2013 meeting.

**Alkyl Betaines**

The Panel requested additional data to support the safety of 11 alkyl betaines. The additional data needed are (1) method of manufacturing, and (2) impurities for the following ingredients:

- betaine
- behenyl betaine
- cetyl betaine
- coco-betaine
- decyl betaine
- hydrogenated tallow betaine
- lauryl betaine
- myristyl betaine
- oleyl betaine
- stearyl betaine
- tallow betaine

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

The Panel reviewed *Rosmarinus officinalis* (Rosemary)-derived ingredients for the first time at this meeting and determined that additional data were needed to make a determination of safety. The Panel is requesting the following:

1. Dermal sensitization data for 10% *rosmarinus officinalis* (rosemary) leaf extract (i.e., a human repeated-insult patch test in a sufficient number of subjects at concentration of use);
2. Chemical characterization of the flower, if available;
3. Additional information on the deodorizing process performed during preparation of some of the ingredients, including information on what by-products may form; and
4. Information as to why the *PDR of Herbal Medicines* states that rosemary preparations should not be used during pregnancy.

The report, as submitted to the Panel, included 12 ingredients. At the meeting, the Panel determined that *rosmarinus officinalis* (rosemary) flower wax should be removed from the report because it is chemically dissimilar from the other ingredients and rosmarinic acid should be removed because it is a constituent that is found in other botanical sources and is not unique to rosemary. The ingredients named below are the 10 *Rosmarinus officinalis* (Rosemary)-derived ingredients currently being evaluated.

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

However, the CIR is in the process of confirming with the Research Institute of Fragrance Materials (RIFM) whether *rosmarinus officinalis* (rosemary) flower/leaf/stem water, *rosmarinus officinalis* (rosemary) leaf water, and *rosmarinus officinalis* (rosemary) water are used as fragrance ingredients only. If their use is as fragrance only, they will be deleted from the conclusion of the safety assessment because they will be under the purview of the RIFM, in accordance with CIR policy.

**Re-review and New Data**

**Iodopropynyl Butylcarbamate**

The Panel reaffirmed the 1996 conclusion that iodopropynyl butylcarbamate is safe as used in cosmetic at concentrations ≤ 0.1%.
The Panel reviewed the Scientific Committee on Cosmetic Products and Non-Food Product’s (SCCNFP) opinion on iodopropynyl butylcarbamate that formed the basis for the EU’s limitations on the use of this ingredient and the EU’s concern about the potential iodine release from this ingredient in product formulations. The Panel stated that missing data and inconsistencies in the results reported in the SCCNFP opinion, e.g., effects on the thyroid gland in rats in a 104-week and a chronic oral toxicity study on this ingredient (up to 80 mg/kg/day), called into question the potential release of iodine from iodopropynyl butylcarbamate in cosmetic products. Thus, the Panel concluded that there was minimal concern about the release of iodine from products containing these ingredients. The Panel also noted that the available irritation and sensitization data do not suggest that iodopropynyl butylcarbamate is unsafe for use in cosmetic products at concentrations up to 0.05%, the highest maximum use concentration reported in a survey of ingredient use concentrations.

Re-review Summaries

The Panel approved the summaries of their actions at the June meeting to not reopen the safety assessments of PVP and Retinol and Retinyl Palmitate.

128th Meeting Notes

Director’s Report

Dr. Gill welcomed the Panel and participants to her inaugural meeting as the new CIR Director. She also introduced Michael Best, Consumer Federation of America, and welcomed his participation at the full Panel meeting.

She discussed the legal opinion from the Council regarding the use of data prepared and submitted to the European Chemical Agency (ECHA) by private companies as part of the REACH chemical registration process, which are available on the ECHA website. CIR requested the opinion because it was unclear from the information provided on the ECHA website whether or not links to the information or use of the information in safety assessments was permissible. The Legal Department concluded that CIR can cite third party scientific studies posted on the ECHA website and use the accompanying robust studies without first gaining permission from the author. The CIR was informed that ECHA legal requirements allow for links from the CIR website to ECHA webpages when ECHA is acknowledged as the source of the link and their legal notice is accessible from the linked page.

Dr. Gill provided an update on the status of the 59 ingredients identified in October 2010 as having insufficient data to support safety. The Panel established a 2-yr window for industry to provide the needed data. On October 8, 2012, 6 ingredients remained on the insufficient data list, and as of this meeting, the safety assessments of 5 of the 6 are either complete or in process. Acrylates/C10-30 alkyl acrylate crosspolymer (polymerized in benzene) will be moved to the Use Not Supported category at the end of September 2013.

Lastly, Dr. Gill mentioned the European Commission’s recent action on methylchloroisothiazolinone and methylisothiazolinone with magnesium chloride and magnesium nitrate. These preservatives continue to be a high priority and CIR encourages all interested parties to provide all available data relevant to the concern about the apparent increase of individuals who have allergic reactions to the preservative.

Reports tabled

Alumina and Aluminum hydroxide

The Panel tabled further discussion of alumina and aluminum hydroxide to allow for a reorganization of the report and a clarification of the presentation of aluminum in the context of the ingredients used in cosmetics.

Although the Panel issued a tentative safety assessment with the conclusion that alumina and aluminum hydroxide are safe in the present practices of use and concentration in cosmetics, the Panel discussed the potential for confusing these ingredients, as used in cosmetics, with elemental or metallic aluminum. Acknowledging the hypothesized connections between aluminum exposures to Alzheimer’s disease and breast cancer, the Panel indicated that these hypotheses are not relevant for the safety assessment of alumina and aluminum hydroxide because, among other reasons, these ingredients are different from elemental or metallic aluminum. Use of alumina and aluminum hydroxide in cosmetics would not result in systemic absorption of aluminum.

Scientific Literature Reviews

- These literature reviews are currently posted on the CIR website at http://www.cir-safety.org/ingredients/glossary/all
  - Camellia sinensis-Derived ingredients
  - Mono- & Disaccharides
  - Pentaerythrityl Tetra-di-t-butyl Hydroxyhydrocinnamate

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 December 9-10, 2013.

In addition, re-reviews of the safety assessments listed below may be considered at the December 2013 meeting:

- Polyvinyl Alcohol
- Sodium alpha-olefin sulfonates
- Hydroquinone and p-Hydroxyanisole
- Alpha-hydroxy Acids
- Tocopherol, to include Tocotrienols

- These literature reviews are currently in preparation
  - Citrus-derived ingredients
  - Hydrogenated Polydecenes
Next CIR Expert Panel Meeting
Monday and Tuesday, December 9-10, 2013 at the Madison Hotel, 1177 Fifteenth Street, NW, Washington, DC 20005 --- Please contact Carla Jackson (jacksonc@cir-safety.org) at CIR before the meeting if you plan to attend.