Announcement

Cosmetic Ingredient Review Expert Panel
138th Meeting (March 31-April 1, 2016) - Findings

April 6, 2016

● Final Safety Assessments
  • Alkonium Clays – 8 ingredients
  • Apple-Derived Ingredients – 26 ingredients
  • 1-Hydroxyethyl-4,5-diamino Pyrazole Sulfate – 1 ingredient
  • Polymerized Tetramethyldicyclosiloxane – 3 ingredients

● Tentative Safety Assessments
  • Chamomilla recutita-Derived Ingredients – 11 ingredients
  • Fatty Acyl Sarcosines & Their Salts – 14 ingredients
  • Helianthus annuus (Sunflower)-Derived Ingredients – 12 ingredients
  • Hexamethylene Diisocyanate (HDI) Polymers – 19 ingredients
  • Keratin and Keratin-Derived Ingredients – 8 ingredients
  • Phosphoric Acid and Simple Salts – 31 ingredients
  • Polyglyceryl Fatty Acid Esters – 274 ingredients
  • Sodium Sulfate – 1 ingredient
  • Trimellitic Anhydride Copolymers – 6 ingredients

● Insufficient Data Announcement
  • Acryloyldimethyltaurate Polymers – 21 ingredients
  • Rosa canina-Derived Ingredients – 12 ingredients

● 138th Meeting Notes
  • Director’s Report
  • Other Items
    o Format
    o Botanical Decision Tree
    o PHMB
  • 2017 Draft Priorities
  • Scientific Literature Reviews posted on the CIR website
  • Scientific Literature Reviews under development
  • Re-reviews for the next Panel meeting
  • Next Expert Panel Meeting – Monday and Tuesday, June 6 – 7, 2016
Final Safety Assessments

Final safety assessments and final amended safety assessments will be posted on the CIR website at www.cir-safety.org. Unpublished data cited as references in CIR safety assessments are available for review. 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.

Alkonium Clays

The Panel issued a final report with the conclusion that the following 8 alkonium clays are safe as used when formulated to be non-irritating:

- Hydrogenated Tallowalkonium Bentonite*
- Quaternium-18/Benzalkonium Bentonite*
- Quaternium-90 Bentonite
- Stearalkonium Bentonite
- Benzalkonium Montmorillonite*
- Quaternium-90 Montmorillonite
- Benzalkonium Sepiolite*
- Quaternium-90 Sepiolite

*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 the products of the cation exchange of an ammonium salt with smectite clays; the alkonium ions are expected to remain absorbed or trapped in the clays in formulation. These ingredients are reported to function as dispersing agents-nonsurfactant, emulsion stabilizers, and viscosity increasing agents-anaqueous.

Stearalkonium Bentonite has the most reported uses at 388, including 385 leave-on uses and 3 rinse-off uses; the majority of these uses are in nail products, but this ingredient is also used in lipstick and eye shadow formulations.

Apple-Derived Ingredients

The Panel issued a final report with the conclusion that the following 21 apple-derived ingredients are safe in the present practices of use and concentration in cosmetics as described in this safety assessment, when formulated to be non-irritating and non-sensitizing. Pyrus malus and Malus domestica are two taxonomic names for apple.

- Pyrus Malus (Apple) Bark Extract*
- Pyrus Malus (Apple) Carpel Powder*
- Pyrus Malus (Apple) Fiber*
- Pyrus Malus (Apple) Flower Extract
- Pyrus Malus (Apple) Fruit Extract
- Pyrus Malus (Apple) Fruit
- Pyrus Malus (Apple) Fruit Water
- Pyrus Malus (Apple) Juice
- Pyrus Malus (Apple) Pectin Extract*
- Pyrus Malus (Apple) Peel Extract*
- Pyrus Malus (Apple) Peel Powder
- Pyrus Malus (Apple) Peel Wax*
- Pyrus Malus (Apple) Pulp Extract*
- Pyrus Malus (Apple) Root Bark Powder*
- Pyrus Malus (Apple) Seed Extract
- Malus Domestica (Apple) Fiber
- Malus Domestica (Apple) Fruit Extract
- Malus Domestica (Apple) Fruit Water
- Malus Domestica (Apple) Fruit Cell Culture Extract
- Malus Domestica (Apple) Juice
- Malus Domestica (Apple) Oil

The Panel concluded that the available data are insufficient for evaluating the safety of the following 5 apple-derived ingredients in cosmetic products:

- Pyrus Malus (Apple) Root Extract
- Pyrus Malus (Apple) Stem Extract*
- Malus Domestica (Apple) Callus Extract*
- Malus Domestica (Apple) Oil
- Malus Domestica (Apple) Stem Extract

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

The data that are needed to evaluate the safety of these 5 ingredients are:

- Method of manufacture and impurities
- 28-day dermal toxicity study; if absorbed, genotoxicity and reproductive and developmental toxicity data may be needed

Apple-derived ingredients are being used in leave-on cosmetic products at maximum ingredient use concentrations up to 9% (Pyrus Malus (Apple) Fruit Water), and in rinse-off cosmetic products at maximum ingredient use concentrations up to 0.8% (Pyrus Malus (Apple) Fruit Extract).

The Panel noted that phloridzin, which is a constituent of apple root bark powder and apple leaf extract, stimulated melanogenesis in vitro. They stated that increased cutaneous pigmentation would not be expected at use concentrations of apple-derived ingredients in cosmetic products. However, manufacturers
should be aware of this potential effect and ensure that formulations that have ingredients containing phloridzin do not stimulate melanogenesis when applied to the skin.

**1-Hydroxyethyl 4,5-Diamino Pyrazole Sulfate**

The Panel issued a final report with the conclusion that 1-Hydroxyethyl 4,5-Diamino Pyrazole Sulfate is safe as an oxidative hair dye ingredient in the present practices of use and concentration.

The Panel noted that the use of oxidative hair dye formulations involves exposure to precursors and coupling agents as well as to their reaction products. While reaction intermediates are formed, human exposure is primarily to the precursors, coupling agents, and reaction products, not to the reaction intermediates. Exposures to the precursors and couplers are low, because they are consumed in the color forming reaction, and exposures to reaction products are even lower, because they are adsorbed onto and physically retained on the hair shaft. Therefore, it was the consensus of the Panel that safety assessments of oxidative hair dyes are primarily determined by the toxicological evaluation of the ingredients (i.e. precursors and coupling agents), and not of the reaction intermediates or products formed during use.

**Polymerized Tetramethylocyclohexasiloxanes**

The Panel issued a final report with the conclusion that the following 3 polymerized tetramethylocyclohexasiloxanes are safe when used to coat metal oxide particles and that the data are insufficient to determine safety if these ingredients are used independently.

- Polysilicone-2
- Polysilicone-4
- Polysilicone-5

The potential for systemic toxicity was not a concern because these silicone polymers and the metal oxide particles that they coat are large and not likely to penetrate the skin, and the results of HRIPT studies were negative.

The *International Cosmetic Ingredient Dictionary and Handbook (Dictionary)* monographs for these ingredients were recently amended to include “surface modifier” as a function. The note “[Ingredient name] may be used as a coating agent polymerized in situ typically on metal oxides or other materials” has been added to the INCI Dictionary entries for each ingredient. The other functions reported for these ingredients, including antifoaming agents, hair conditioning agents, and viscosity increasing agents – nonaqueous, do not appear to be compatible with the use of large surface-coated particles as cosmetic ingredients, but these functions have not been removed from the INCI Dictionary. The chemical forms of the ingredients purported to serve these other functions have not been defined in the INCI Dictionary and have not been considered further in this report.

The data needed to determine the safe use of these 3 ingredients for functions other than to coat metal oxide particles are:

- Chemistry, including average molecular weight and distribution, and method of manufacture
- Repeated dose inhalation
- Absorption/metabolism; if dermally absorbed, then reproductive toxicity, 28-day dermal toxicity, and genotoxicity may be needed
- Impurity data for all three ingredients

**Tentative Safety Assessments**

*Tentative and revised tentative safety assessments will be posted on the CIR website at [www.cir-safety.org](http://www.cir-safety.org) on or before April 13, 2016.* 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 June 7, 2016 or as soon as possible. If comments are received before May 30, 2016, the updated reports may be scheduled for review by the CIR Expert Panel at its June 6–7, 2016 meeting.

**Chamomilla recutita-Derived Ingredients**

The Panel issued a tentative amended report for public comment with the conclusion that the following 11 *Chamomilla recutita*-derived ingredients are safe in the present practices of use and concentration in cosmetics as described in this safety assessment, 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
- 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

*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 data submitted to support the safety of 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, which were found to be insufficient at the December 9-10, 2013 CIR Expert Panel meeting. The Panel determined that the additional data support revising the previous conclusion to indicate that all of the ingredients in this report are safe as used when formulated to be nonsensitizing, including these 6 ingredients.
Fatty Acyl Sarcosines and Their Salts

The Panel issued a tentative amended report for public comment with the conclusion that the following 10 previously reviewed fatty acyl sarcosines and their salts, and 4 salts that have not been reviewed previously by the Panel, are safe as used in cosmetics when formulated to be non-irritating; these ingredients should not be used in cosmetic products in which N-nitroso compounds may be formed:

**Previously Reviewed**

- Cocoyl Sarcosine
- Lauroyl Sarcosine
- Myristoyl Sarcosine
- Oleoyl Sarcosine
- Stearoyl Sarcosine
- Ammonium Cocoyl Sarcosinate*
- Ammonium Lauroyl Sarcosinate
- Sodium Cocoyl Sarcosinate
- Sodium Lauroyl Sarcosinate
- Sodium Myristoyl Sarcosinate

**Additional Salts**

- Potassium Cocoyl Sarcosinate*
- Potassium Lauroyl Sarcosinate*
- Sodium Oleoyl Sarcosinate*
- Sodium Palmitoyl Sarcosinate

*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 had concluded (published in 2001) that the 10 previously reviewed ingredients were safe as used in rinse-off products and safe for use in leave-on products at concentrations of ≤5%, but the data were insufficient to determine safety for use in products that are likely to be inhaled, and these ingredients should not be used in cosmetic products in which N-nitroso compounds may be formed. The 5% concentration limit had been established for leave-on products, based upon the highest concentration tested in human repeat-insult patch tests, because concentration of use data were not provided at the time of the original safety assessment.

The Panel removed the 5% restriction for leave-on products because sensitization was not observed in studies at the highest concentration currently reported to be used.

The Panel discussed a photosensitization study indicating that Oleoyl Sarcosine may possess photocontact-allergenic potential in guinea pigs. The Panel noted that the chemical structure of Oleoyl Sarcosine does not have a chromophore, so there are no structural alerts for photosensitization. Additionally, the study did not indicate that an unirradiated control was used. The Panel stated that the allergenic response observed in the study was most probably due to a contaminant, not to Oleoyl Sarcosine.

**Helianthus annuus (Sunflower)-Derived Ingredients**

The Panel issued a tentative report for public comment with the conclusion that the following 9 *Helianthus annuus* (sunflower)-derived ingredients are safe in the present practices of use and concentration in cosmetics as described in this safety assessment; however, persons with known allergies to nut or seed proteins should avoid using personal care products that contain these ingredients:

- Helianthus Annuus (Sunflower) Seed Extract
- Helianthus Annuus (Sunflower) Flower Extract
- Helianthus Annuus (Sunflower) Seed
- Helianthus Annuus (Sunflower) Seed Butter*
- Helianthus Annuus (Sunflower) Seedcake
- Helianthus Annuus (Sunflower) Seed Flour*
- Helianthus Annuus (Sunflower) Seed Wax
- Hydrogenated Sunflower Seed Extract*
- Hydrolyzed Sunflower Seed Wax

*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 concluded that the available data are insufficient for evaluating the safety of the following 3 *Helianthus annuus* (sunflower)-derived ingredients in cosmetic products:

- Helianthus Annuus (Sunflower) Extract
- Helianthus Annuus (Sunflower) Leaf/Stem Extract*
- Helianthus Annuus (Sunflower) Sprout Extract*

The additional data needed include:

- Method of manufacture
- Composition of these ingredients, especially protein content (including 2S albumin)
- Impurities

The Panel discussed the potential for proteins of the 2S-albumin fraction of sunflower seeds to cause IgE-mediated-immediate (Type I) hypersensitivity reactions. Although these reactions have not been observed in their clinical experience, Panel members decided that the information on the potential for 2S proteins from nuts and seeds to cause Type 1 hypersensitivity reactions warranted a cautionary statement.

**Hexamethylene Diisocyanate (HDI) Polymers**

The Panel issued a revised tentative report for public comment with the conclusion that the following 17 hexamethylene diisocyanate (HDI) polymers are safe as used:

- HDI/Trimethylol Hexyllactone Crosspolymer
- Bis-C16-20 isoalkoxy TMHD/PEG-90 Copolymer
- Bis-Isostearyl 1,4-Butanediol/HDI/Hydrogenated Dimer Dilinoleyl Alcohol Copolymer*
Bis-Lauryl Cocaminopropylamine/HDI/PEG-100 Copolymer*  HDI/PPG/Polycaprolactone Crosspolymer  
Bis-Methoxy PEG-10 Dimethyl MEA/HDI/Bis-PEG-10 Dimethicone Copolymer*  Methoxy PEG-17/Methoxy PEG-11/HDI Isocyanurate Trimer  
Cholesterol/HDI/Pullulan Copolymer*  Methoxy PEG-17/Methoxy PEG-11/HDI Crosspolymer  
Decyl HDI/PEG-180 Crosspolymer*  PEG-240/HDI Copolymer Bis-Deetyl tetradeceth-20 Ether  
Diethylene Glycol/DMAP Acrylamide/PEG-180/HDI Copolymer  PPG-26/HDI Copolymer*  
HDI/Di-C12-14 Alkyl Tartrate/Hydrogenated Dilinoleyl Alcohol Copolymer  Steareth-100/PEG-136/HDI Copolymer  
HDI/PEI-45/SMDI Crosspolymer*  Stearyl HDI/PEG-50 Copolymer*  
Methoxy PEG-17/Methoxy PEG-11/HDI Crosspolymer  
PEG-240/HDI Copolymer Bis-Decyltetradeceth-20 Ether  
PPG-26/HDI Copolymer*  
Steareth-100/PEG-136/HDI Copolymer  
Stearyl HDI/PEG-50 Copolymer*  

*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 concluded that the available data are insufficient for evaluating the safety of the following 2 hexamethylene diisocyanate (HDI) polymers in cosmetic products:

Bis-Hydroxyethyl Acrylate Poly(1,4-Butanediol)-9/TMHDI Copolymer*  
1,4-Butanediol/Succinic Acid/Adipic Acid/HDI Copolymer*  

The data needed to evaluate the safety of these 2 ingredients include:

- Molecular weight range (i.e., median MW and distribution)
- If the molecular weight is below 1000 Da, then solubility in formulation, dermal absorption, and/or 28-day dermal toxicity data may be needed
- If soluble or dermally absorbed, then systemic toxicity, including genotoxicity, carcinogenicity, and reproduction/developmental toxicity

HDI/Trimethylol Hexyllactone Crosspolymer has the greatest number of cosmetic uses, and is used in up to 385 formulations. It also has the highest concentration of use for leave-on products, i.e. 31%.

Exposure to diisocyanates (such as HDI) in the workplace is one of the leading causes of occupational asthma and has been associated with airway irritation and asthma-like symptoms, hypersensitivity pneumonitis, rhinitis, and accelerated lung deterioration. Diisocyanates can also cause both irritant and allergic contact dermatitis, as well as skin and conjunctival irritation. The data showed that the diisocyanate monomers would not be present in the ingredients as manufactured, but the Panel stressed that the cosmetics industry should use good manufacturing practices to ensure that these monomers are not present in the ingredient or in formulation.

**Keratin and Keratin-Derived ingredients**

The Panel issued a tentative report for public comment with the conclusion that the following 8 keratin-derived ingredients are safe in cosmetics in the present practices of use and concentration as described in this safety assessment.

- Hydrolyzed Keratin
- Hydrolyzed Hair Keratin
- Hydrolyzed Oxidized Keratin*
- Hydrolyzed Sulfonated Keratin*
- Keratin
- Oxidized Keratin*
- Soluble Keratin
- Sulfonated Keratin*

*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.

Pesticide residues and heavy metals may be present in keratin source materials. The Panel stressed that the cosmetics industry should continue to use the necessary procedures to limit these impurities in the ingredients before blending into cosmetic formulations.

The Panel was also concerned about the inherent risks of using animal- and human-derived ingredients in cosmetic products, namely the potential for transmission of infectious agents. The Panel stressed that these ingredients must be free of detectible infectious pathogens (e.g. Bovine Spongiform Encephalopathy (BSE), Human Immunodeficiency Virus (HIV), and Creutzfeld-Jacob disease (CJD)). Suppliers and users of these ingredients must assure that these ingredients are free from pathogenic viruses or infectious agents.

**Phosphoric Acid and Simple Salts**

The Panel issued a tentative report for public comment with the conclusion that the following 31 ingredients are safe in the present practices of use and concentration in cosmetics as described in this safety assessment, when formulated to be non-irritating.

<table>
<thead>
<tr>
<th>Phosphoric Acid</th>
<th>Disodium Phosphate</th>
<th>Potassium Polyphosphate*</th>
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</thead>
<tbody>
<tr>
<td>Ammonium Phosphate</td>
<td>Disodium Pyrophosphate</td>
<td>Sodium Hexametaphosphate</td>
</tr>
<tr>
<td>Dicalcium Phosphate</td>
<td>Magnesium Hydrogen Phosphate*</td>
<td>Sodium Metaphosphate</td>
</tr>
<tr>
<td>Calcium Dihydrogen Phosphate</td>
<td>Magnesium Phosphate*</td>
<td>Sodium Polyphosphate*</td>
</tr>
<tr>
<td>Calcium Phosphate</td>
<td>Metaphosphoric Acid*</td>
<td>Sodium Phosphate</td>
</tr>
<tr>
<td>Calcium Potassium Sodium Phosphate*</td>
<td>Pentapotassium Triphosphate</td>
<td>Sodium Trimetaphosphate*</td>
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<tr>
<td>Calcium Pyrophosphate</td>
<td>Pentasodium Triphosphate*</td>
<td>Tetrapotassium Pyrophosphate</td>
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<td>Diammonium Phosphate</td>
<td>Phosphate Buffered Saline*</td>
<td>Tricalcium Phosphate</td>
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<tr>
<td>Dicalcium Phosphate Dihydrate</td>
<td>Potassium Metaphosphate</td>
<td>Trimagnesium Phosphate</td>
</tr>
<tr>
<td>Dipotassium Phosphate</td>
<td>Potassium Phosphate</td>
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</tr>
</tbody>
</table>
Trisodium 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 the broad range of results (from no irritation to corrosive effects) reported for phosphoric acid or its salts at concentrations including concentrations that are used in cosmetic products. The survey provided in 2015 indicated that Disodium Phosphate had the highest maximum concentration of use (58%) in leave-on products (i.e., face and neck products [not spray]). Recent data indicate a reduction in the maximum use concentration of Disodium Phosphate to 1.2%. However, Dicalcium Phosphate Dihydrate is used in dentifrices (rinse-off products) at concentrations up to 49%.

The Panel discussed studies that show Potassium Phosphate-induced renal damage and, in some cases, renal cancer in animals. They noted that oral exposures to Potassium Phosphate promoted the development of kidney tumors initiated by treatment with a renal carcinogen. The Panel also discussed human epidemiological studies on potassium phosphate indicating that this salt was not associated with renal damage or cancer. The Panel concluded that renal toxicity/carcinogenicity would not result from human exposure to a cosmetic product containing phosphoric acid or its salts.

The Panel agreed that the form of Phosphoric Acid used as an ingredient in cosmetic products should be specified in this report. For example, phosphoric acid can exist in the ortho, meta, and para configurations. In addition, they noted the possibility that the INCI ingredient name for Ammonium Phosphate is actually ammonium dihydrogen phosphate. The panel agreed that this safety report should provide appropriate names and other identifying information for the ingredient and asked the Industry to clarify the chemical structure provided in the INCI Dictionary.

Polyglyceryl Fatty Acid Esters

The Panel issued a tentative report for public comment with the conclusion that the following 274 polyglyceryl fatty acid esters are safe as used in cosmetics when formulated to be non-irritating:

<table>
<thead>
<tr>
<th>Ingredient Name</th>
<th>INCI Name</th>
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<tbody>
<tr>
<td>Adansonia Digitata Seed Oil Polyglyceryl-6 Esters*</td>
<td>Polyglyceryl-2 Isopalmitate/Sebacate*</td>
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<td>Almond Oil/Polyglyceryl-10 Esters*</td>
<td>Polyglyceryl-2 Isostearate</td>
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<td>Apricot Kernel Oil Polyglyceryl-3 Esters*</td>
<td>Polyglyceryl-2 Laurate</td>
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<td>Polyglyceryl-2 Isopalmitate*</td>
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</table>

The Panel issued a tentative report for public comment with the conclusion that the following 274 polyglyceryl fatty acid esters are safe as used in cosmetics when formulated to be non-irritating:
Polyglyceryl-20 Docosabehenate/Oleate*  Shea Butter Polyglyceryl-4 Esters*
Polyglyceryl-20 Heptacyclate* Shea Butter Polyglyceryl-6 Esters*
Polyglyceryl-20 Heptadecabehenate/Laurate* Soybean Oil Polyglyceryl-6 Esters*
Polyglyceryl-20 Hexacyclate* Sunflower Seed Oil Polyglyceryl 3 Esters*
Polyglyceryl-20 Octadecabehenate/Laurate* Sunflower Seed Oil Polyglyceryl-4 Esters*
Polyglyceryl-20 Octaionanonanoate* Sunflower Seed Oil Polyglyceryl-5 Esters*
Pumpkin Seed Oil Polyglyceryl-4 Esters* Sunflower Seed Oil Polyglyceryl-6 Esters*
Pumpkin Seed Oil Polyglyceryl-4 Esters* Sweet Almond Oil Polyglyceryl-4 Esters*
Safflower Oil Polyglyceryl-6 Esters* Sweet Almond Oil Polyglyceryl-6 Esters*
Sclerocarya Birrea Seed Oil Polyglyceryl-6 Esters* Theobroma Grandiflorum Seed Butter Polyglyceryl-6 Esters*
Sclerocarya Birrea Seed Oil Polyglyceryl-10 Esters* Trichilia Emetica Seed Oil Polyglyceryl-4 Esters*
Sesame Oil Polyglyceryl-6 Esters* Watermelon Seed Oil Polyglyceryl-6 Esters*
Shea Butter Polyglyceryl-3 Esters* Watermelon Seed Oil Polyglyceryl-10 Esters*

*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 ingredients in this report are esterification products of polyglycerin chains and fatty acids. They vary in numbers of glycerin and fatty-acid equivalents and lengths of the fatty acids. The polymerization process used to produce polyglycerol yields a distribution of oligomers with primarily linear structures. In addition to the linear configurations, a significant part of the polyglycerol polymer products is branched, originating, e.g., from 1,2- and 2,2-O-ether linkages.

The Panel acknowledged that some of these ingredients can be penetration enhancers, and care should be taken when formulating cosmetic products containing these ingredients combined with ingredients the safety of which was based, at least partially, on data or other information indicating the lack of dermal absorption, or for which the potential for dermal absorption and systemic toxicity was a concern. The Panel also noted that some of these ingredients are derived from plants, and expressed concern about pesticide residues and heavy metals that may be present in botanical ingredients; the Panel stressed that the cosmetics industry should continue to use the necessary procedures to limit these impurities in the ingredient before blending into cosmetic formulations.

The Panel has previously reviewed the safety of several ingredients that serve as starting materials for the synthesis of polyglyceryl fatty acid esters, and may persist as residual impurities in the polyglyceryl esters products or may represent potential metabolites (e.g., glycerin and free fatty acids released by the action of esterases in the skin. Acacia Decurrens/Jojoba/Sunflower Wax Polyglyceryl-3 Esters was removed from the report because the Panel previously found the data insufficient to support the safety of Acacia Decurrens Extract in cosmetic formulations.

Finally, the Panel noted that the fatty-acid composition profile is missing for several ingredients in this report. The Panel would appreciate submission of such data for these ingredients.

**Sodium Sulfate**

The Panel issued a tentative amended report for public comment with the conclusion that Sodium Sulfate is safe as used in cosmetics when formulated to be non-irritating. The Panel reopened the Safety Assessment of Sodium Sulfate (published in 2000) based on a significant increase in frequency of use, as compared to the original report, and an increase in the highest maximum use concentration in leave-on cosmetic products, which exceeds the corresponding concentration presented in the original report.

In 2000, data from the Food and Drug Administration (FDA) Voluntary Cosmetic Registration Program (VCRP) recited frequency of use of Sodium Sulfate in cosmetic formulations to be 28. In 2016, the VCRP data recites 777 uses for Sodium Sulfate in cosmetic formulations: 86 in leave-on, 661 in rinse-off, and 30 in bath products.

The Panel concluded in 2000 that Sodium Sulfate was safe for use in rinse-off formulations, and safe at concentrations up to 1% in leave-on formulations. The concentrations of use reported in the original safety assessment were obtained from industry in two separate submissions of unpublished data. These data are considered to be a limited representation of concentrations in use at that time. The highest reported maximum use concentration of Sodium Sulfate in a leave-on cosmetic product in the original report was 0.5% (in a facial lotion and facial toner). In comparison, the 2015-2016 industry survey indicates that the highest maximum use concentration of Sodium Sulfate in a leave-on cosmetic product is 2.0% (in hair tonics and other hair grooming aids).

**Trimellitic Anhydride Copolymers**

The Panel noted the lack of data in this safety assessment and expressed concern that these copolymers are essentially chemically undefined. In the absence of fundamental data about the chemistry of these ingredients, safety cannot be evaluated for the use of these copolymers in any type of cosmetic formulation. Therefore, the Panel amended its previous conclusion of safe in nail products and insufficient data for use in all other types of cosmetic formulations, and issued a tentative amended report with a conclusion that the data are insufficient to support the safety of the 6 ingredients named below under conditions of intended uses.

- Adipic Acid/CHDM/MA/Neopentyl Glycol/Trimellitic Anhydride Copolymer*
- Adipic Acid/Neopentyl Glycol/Trimellitic Anhydride Copolymer
- Isostearoyl Trimellitic Anhydride/Trimethylolpropane Copolymer*
- Phthalic Anhydride/Trimellitic Anhydride/Glycols Copolymer
- Propylene Glycol/Sesamic Acid/Trimellitic Anhydride Copolymer*
- Trimethylpentanediol/Isophthalic Acid/Trimellitic Anhydride Copolymer*

* Not reported to be in current use.

The following are needed to evaluate the safety of these ingredients in nail products:

- Method of manufacture; and
In addition, the following are needed to evaluate the safety of these ingredients in cosmetics other than nail products:

- Molecular weight;
- Impurities, specifically, the amount of residual monomer in each copolymer
- Metabolism, specifically, whether these ingredients are metabolized in the skin;
- Dermal absorption; if absorbed, then genotoxicity and reproductive toxicity data are needed; and
- Dermal irritation and sensitization at maximum leave-on concentration of use.

Based on data from the FDA VCRP and the Council concentration of use survey, two of the trimellitic anhydride copolymers are reported to be in use. Both sources report that these ingredients are used in nail formulations, but only the VCRP data indicate that one of these ingredients is used in formulations that result in dermal contact.

**Insufficient Data Announcement**

*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 August 5, 2016. These reports will be scheduled for review by the CIR Expert Panel at its September 26-27, 2016 meeting.*

**Acryloyldimethyltaurate Polymers**

The Panel issued an insufficient data announcement for the following 21 ingredients:

- Acrylamide/Sodium Acryloyldimethyltaurate Copolymer
- Dimethylacrylamide/Sodium Acryloyldimethyltaurate Crosspolymer
- Acrylamide/Sodium Acryloyldimethyltaurate/Acrylic Acid Copolymer
- HEA/Sodium Acryloyldimethyltaurate/Steareth-20 Methacrylate Copolymer
- Ammonium Acryloyldimethyltaurate/Beheneth-25 Methacrylate Crosspolymer
- Hydroxyethyl Acrylate/Sodium Acryloyldimethyl Taurate Copolymer
- Ammonium Acryloyldimethyltaurate/Carboxyethyl Acrylate Crosspolymer
- Sodium Acrylate/Acryloyldimethyltaurate/Dimethylacrylamide Crosspolymer
- Ammonium Acryloyldimethyltaurate/Laureth-7 Methacrylate Copolymer
- Sodium Acrylate/Sodium Acryloyldimethyl Taurate Copolymer
- Ammonium Acryloyldimethyltaurate/Steareth-25 Methacrylate Crosspolymer
- Sodium Acrylate/Sodium Acryloyldimethyl Taurate/Acrylamide Copolymer
- Ammonium Acryloyldimethyltaurate/Vinyl Formamide Copolymer
- Sodium Acryloyldimethyltaurate/PEG-8 Diacrylate Crosspolymer
- Ammonium Polyacryloyldimethyl Taurate
- Sodium Acryloyldimethyltaurate/VP Crosspolymer

The additional data needed are:

- Molecular weight ranges
- Impurities data, including data on any residual acrylamide, vinyl formamide, and methacrylamidolauric acid monomers
- Sensitization data for Hydroxyethyl Acrylate/Sodium Acryloyldimethyl Taurate Copolymer at 4.3% or greater

**Rosa canina-Derived Ingredients**

The Panel issued an insufficient data announcement for the following 9 ingredients:

- Rosa Canina Bud Extract
- Rosa Canina Leaf Extract
- Rosa Canina Flower
- Rosa Canina Seed
- Rosa Canina Flower Extract
- Rosa Canina Seed Extract
- Rosa Canina Flower Oil
- Rosa Canina Seed Oil
- Rosa Canina Flower Powder
- Rosa Canina Seed Powder

The data that are needed to evaluate the safety of these 9 ingredients are:

- Method of manufacture
- Composition and impurities
- Use concentration data on Rosa Canina Bud Extract, Rosa Canina Flower Oil, Rosa Canina Flower Powder, Rosa Canina Fruit Juice, Rosa Canina Leaf Extract, Rosa Canina Seed, and Rosa Canina Seed Powder
- 28-day dermal toxicity data
- Skin irritation and sensitization data
138th Meeting Notes

Director’s Report

Dr. Gill noted the passing of William W. Carlton, D.V.M., Ph.D. Dr. Carlton was appointed to the CIR Expert Panel in 1982 and was a dedicated contributor to the Panel for 18 years. The Panel observed a moment of silence offered by Dr. Bergfeld at the beginning of the Panel meeting.

Dr. Gill welcomed Dr. Jack Linard of Unilever to the Panel meeting. Dr. Linard is the new Chair of the CIR Science and Support Committee (CIR SSC).

CIR staff co-authored 2 Posters that were presented at the 2016 Society of Toxicology meeting in New Orleans. Dr. Ivan Boyer and Dr. Bart Heldreth contributed to the poster titled **COSMOS DB as an International Share Point for Exchanging Safety Evaluation and Toxicity Data, and Expanding the Known Chemical Space**, which announces the release of version 2 of the COSMOS DB. Version 2 now includes a safety evaluation section. In addition, Drs. Boyer and Heldreth contributed to the poster titled **Read-Across at the Crossroads of Chemoinformatics and Regulatory Science: A Case study at Cosmetic Ingredient Review**. The development of this poster involved using the Alkyl PEG Ether ingredient group in a case study that focused on skin irritation and sensitization as target endpoints.

Later this month, CIR staff will present the CIR ingredient safety-assessment process in other national and international fora. Monica Fiume is an invited speaker at the 4th Cosmetic Compliance West Coast seminar and Dr. Heldreth has been invited to discuss the CIR safety assessment process at the 26th Plenary meeting sponsored by the Council of Associations of the Latin American Cosmetic, Personal Care and Home Care Industry (CASIC) in Mexico City.

Other Items

The Panel reviewed a draft final version of the revised CIR report format. Comments provided by the CIR SSC were also discussed.

The Panel discussed revisions to the CIR Aerosols Precedents Document and Framework to address potential inhalation exposures to respirable particles from the use of loose cosmetic powders. The revisions of the Framework will be incorporated, as appropriate, into future safety assessments.

The Panel also responded to the CIR staff request for guidance on two ingredient strategies, one for *Ginkgo biloba* and the other for Polyaminopropyl Biguanide (PHMB). The Panel was asked to provide input on a proposed strategy for preparing a safety assessment of cosmetic botanical ingredients derived from *Ginkgo biloba*. Specifically, the Panel was asked whether the decision tree proposed by the CIR SSC for assessing the safety of botanical cosmetic ingredients can be used to develop CIR safety assessments. The Panel agreed with the proposal to use of *Ginkgo biloba* as a case study to help evaluate the useability and usefulness of the decision-tree tool, and asked Industry to clarify Step 3, named “Assess local tolerance.”

Finally, the Panel was asked to provide input on a review strategy for the cosmetic preservative Polyaminopropyl Biguanide (PHMB). The frequency of use of this ingredient is below the threshold to be considered for developing the list of 2017 Priority ingredients. However, the CIR Expert Panel was asked whether the review of PHMB should be advanced as a priority ingredient because it is currently being considered “not safe for consumers when used as a preservative in all cosmetic products up to the maximum concentration of 0.3%,” by the European Commission’s Scientific Committee on Consumer Safety (SCCS). The CIR Expert Panel agreed that the review of this ingredient should be accelerated as much as possible, considering the time required to obtain the data needed.

Draft 2017 Ingredient Review Priorities

Interested parties are invited to comment on the inclusion of the ingredients listed below as 2017 CIR Draft Priorities. Selection of these ingredients is based on ingredients that have not yet been reviewed by the CIR Expert Panel and have the greatest number of 2016 VCRP uses. Comments are sought also on the additional ingredients that might be included in each ingredient family. Proposed ingredient families may be found, starting at page 22, at the following url: [http://www.cir-safety.org/sites/default/files/admin_2.pdf](http://www.cir-safety.org/sites/default/files/admin_2.pdf). It is likely that not all of the ingredients listed will be chosen for work in 2017. CIR plans to finalize the proposed 2017 priority list at the June 2016 meeting.

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Number of formulations containing ingredient</th>
</tr>
</thead>
<tbody>
<tr>
<td>BENZYL SALICYLATE</td>
<td>2617</td>
</tr>
<tr>
<td>AMMONIUM HYDROXIDE</td>
<td>1347</td>
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<tr>
<td>AMMONIA</td>
<td>599</td>
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<tr>
<td>CAFFEINE</td>
<td>927</td>
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<tr>
<td>SODIUM METHYLPARABEN</td>
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<tr>
<td>HYDROXYETHYL UREA</td>
<td>430</td>
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<tr>
<td>GLYCINE MAX (SOYBEAN) SEED EXTRACT</td>
<td>387</td>
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<tr>
<td>POLYMETHYL SILSESQUIOXANE</td>
<td>376</td>
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<tr>
<td>PTFE</td>
<td>373</td>
</tr>
<tr>
<td>TRIPHENYL PHOSPHATE</td>
<td>353</td>
</tr>
<tr>
<td>SODIUM PHYTATE</td>
<td>330</td>
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<tr>
<td>HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER</td>
<td>328</td>
</tr>
<tr>
<td>EUCALYPTUS GLOBULUS (EUCALYPTUS) LEAF OIL</td>
<td>319</td>
</tr>
<tr>
<td>COCAMIDOPROPYL HYDROXYZULTAINE</td>
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<tr>
<td>POLYURETHANE-11</td>
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<tr>
<td>ZINC GLUCONATE</td>
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<tr>
<td>EUTERPE OLERACEA FRUIT EXTRACT</td>
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<tr>
<td>SCUTELLARIA BAICALENSIS (CHINESE SKULLCAP) ROOT EXTRACT</td>
<td>280</td>
</tr>
</tbody>
</table>
Scientific Literature Reviews

- These literature reviews are currently posted on the CIR website at http://www.cir-safety.org/ingredients/glossary/all
  - Alkoxy Alkyl Silanes
  - Butyrospermum Parkii (Shea)-Derived Ingredients
  - Dialkyl Carbonates
  - Saccharide Esters
  - Simple Carbonate Salts

Draft reports for these ingredient families, along with any unpublished data submitted by interested parties, may be presented to the Panel as soon as at its meeting on June 6-7, 2016.

- These literature reviews are currently under development and may be announced during the first half of 2016.
  - Alkane Diols
  - Alkoxylated Fatty Amides
  - Brown Algae ingredients
  - Etidronic Acid and Its Simple Salts
  - Ethers of Ascorbate
  - Ethers, ester, & salts Panthenol and Pantothenic Acid
  - Ginkgo biloba-Derived Ingredients
  - Humulus lupulus (Hops)-Derived Ingredients
  - Hydrofluorocarbon 152A
  - Melaleuca alternifolia (Tea Tree)-Derived Ingredients
  - Monoalkylglycol Dialkyl Acid Esters
  - Tetrafluoropropene

- Re-reviews scheduled for the next Panel meeting
  - Acid Violet 43
  - Ammonium, Potassium and Sodium Persulfate
  - Butyl Poloxyalkylene Ethers
  - PEG Propylene Glycol Esters

Next CIR Expert Panel Meeting

Monday and Tuesday, June 6-7, 2016, at The Melrose Georgetown Hotel, Washington, DC 20037 --- Please contact Carla Jackson (jacksone@cir-safety.org) before the meeting if you plan to attend.