Announcement

Cosmetic Ingredient Review Expert Panel
135th Meeting (June 15-16, 2015) - Findings

June 19, 2015

• Final Safety Assessments
  • *Centella asiatica*-Derived Ingredients – 9 ingredients
  • PEGs Cocamine – 47 ingredient
  • Polyenes – 26 ingredients
  • Polysorbates – 80 ingredients

• Tentative Safety Assessments
  • *Citrus* Fruit-Derived Ingredients – 80 ingredients
  • Nonoxynols – 27 ingredient
  • Polysaccharide Gums – 106 ingredients
  • Soy Proteins and Peptides – 6 ingredients
  • Trialkyl Trimellitates – 5 ingredients

• Insufficient Data Announcement
  • Alkonium Clays – 8 ingredients
  • *Pyrus malus*-Derived Ingredients – 28 ingredients
  • Silk Proteins – 10 ingredients

• Re-review Summaries
  • Re-review summaries for Bisabolol and Isostearamidopropyl Morpholine Lactate – approved

• 135th Meeting Notes
  • Director’s Report
  • Scientific Literature Reviews posted on the CIR website
  • Scientific Literature Reviews under development
  • Re-reviews for the next Panel meeting
  • 2016 Final Ingredient Review Priorities
  • Next Expert Panel Meeting – Monday and Tuesday, September 21-22, 2015

Final Safety Assessments

*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). Unpublished data cited as references in CIR safety assessments are available for review.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.*

*Centella asiatica* – Derived Ingredients

The Panel issued a final report with the conclusion that the following 9 ingredients are safe in the present practices of use and concentrations in cosmetic products when formulated to be non-sensitizing.

- *centella asiatica* extract
- *centella asiatica* callus culture
- *centella asiatica* leaf extract
- *centella asiatica* flower/leaf/stem extract
- *centella asiatica* leaf cell culture extract
- *centella asiatica* leaf water
- *centella asiatica* meristem cell culture
- *centella asiatica* meristem cell culture extract
- *centella asiatica* root extract
In a briefing on plant cell cultures, an Industry expert stated that centella asiatica meristem cell culture consists of primary metabolites (lipids and glucides), amino acids, and secondary metabolites, and that 20% centella asiatica meristem cell culture was not toxic in a human repeated insult patch test or in *in vitro* ocular irritation, phototoxicity, and genotoxicity tests. Additional information suggested that the composition of centella asiatica meristem cell culture and centella asiatica callus culture are comparable, that the root, stem, and leaves are similar in terms of their composition, and that the greatest concentration of components (e.g., terpenoids and flavonoids) is found in the leaf.

Centella asiatica extract was a reproductive toxicant in male rats at daily oral doses ranging from 100 to 300 mg/kg/day, as was centella asiatica leaf extract at a daily oral dose of 100 mg/kg/day. However, the Panel noted that these levels of exposure would not be approached with ingredient use in a cosmetic product, and the Panel was not concerned about the toxicity risk at the levels reported in this safety assessment.

**PEGs Cocamine and Related Ingredients**

The Panel issued a final amended report with the conclusion that the following 47 PEGs cocamine and related ingredients are safe in cosmetics in the present practices of use and concentration when formulated to be non-irritating:

- PEG-2 cocamine
- PEG-3 cocamine*
- PEG-4 cocamine*
- PEG-5 cocamine
- PEG-8 cocamine*
- PEG-10 cocamine*
- PEG-12 cocamine*
- PEG-15 cocamine
- PEG-20 cocamine*
- PEG-2 hydrogenated tallow amine*
- PEG-5 hydrogenated tallow amine
- PEG-8 hydrogenated tallow amine*
- PEG-10 hydrogenated tallow amine*
- PEG-15 hydrogenated tallow amine*
- PEG-20 hydrogenated tallow amine*
- PEG-30 hydrogenated tallow amine*
- PEG-40 hydrogenated tallow amine*
- PEG-50 hydrogenated tallow amine*
- PEG-2 lauramine*
- PEG-2 oleamine
- PEG-5 oleamine*
- PEG-6 oleamine*
- PEG-10 oleamine*
- PEG-15 oleamine*
- PEG-2 stearamine*
- PEG-5 stearamine*
- PEG-10 stearamine*
- PEG-15 stearamine*
- PEG-50 stearamine*
- PEG-2 tallow amine
- PEG-7 tallow amine*
- PEG-11 tallow amine*
- PEG-15 tallow amine*
- PEG-20 tallow amine*
- PEG-22 tallow amine*
- PEG-25 tallow amine*
- PEG-30 tallow amine*

*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.

Although data gaps were noted, the data available for some of these ingredients and their analogs, together with the SAR-based read-across analysis presented, were used to support the safety of the PEGs cocamine and other related ingredients in this report. The Panel noted that exposure durations and frequencies for the smaller ingredients in this group (i.e., PEG-2, 3, 4, and 5 cocamine and related ingredients) would be relatively low, because these ingredients are used predominantly in rinse-off hair-coloring products.

**Polyenes**

The Panel issued a final safety assessment with the conclusion that the following 26 polyenes are safe in cosmetics in the present practices of use and concentration:

- butene/propylene copolymer*
- butylene/ethylene copolymer
- butylene/ethylene/propylene copolymer
- decene/butene copolymer
- ethylene/octene copolymer*
- ethylene/propylene copolymer
- hydrogenated poly(C6-12 olefin)
- hydrogenated poly(C6-14 olefin)
- hydrogenated poly(C6-20 olefin)
- hydrogenated polybutene*
- hydrogenated polydecene
- hydrogenated polydodecene*
- hydrogenated polyisobutene
- isobutylene/isoprene copolymer*
- isoprene/pentadiene copolymer*
- poly(C4-12 olefin)*
- poly(C6-14 olefin)*
- poly(C20-28 olefin)*
- polydecene
- polyethylene
- polyisobutene
- polyisoprene
- polypropylene
- polypropylene

*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 polyenes exhibited low systemic toxicity at high doses in single-dose and repeated-dose animal studies, no teratogenic or carcinogenic effects in animal studies, and no genotoxicity in *in vitro* and *in vivo* studies. The data indicated use concentrations as high as 95% in lipsticks, however minimal toxicity was observed in repeated dose studies and no irritation or sensitization was observed in multiple animal and human tests at concentrations as high as 100%. The Panel noted that, although molecular weights are in the range that could be dermally absorbed, the lack of heteroatom functional groups dramatically limits solubility and would prevent significant absorption. The lack of such functional groups also limits interactions with other biomolecules and probably accounts for the apparent biological inertness of these ingredients.
Polysorbates

The Panel issued a final amended report with the conclusion that the 80 polysorbates listed below are safe in cosmetics in the present practices of use and concentration when formulated to be non-irritating.

- polysorbate 20
- polysorbate 21
- polysorbate 40
- polysorbate 60
- polysorbate 61
- polysorbate 65
- polysorbate 80
- polysorbate 81
- polysorbate 85
- PEG-30 sorbitan beeswax
- PEG-20 sorbitan cocoate
- PEG-40 sorbitan dioleate
- PEG-2 sorbitan isostearate*
- PEG-5 sorbitan isostearate*
- PEG-20 sorbitan isostearate
- PEG-40 sorbitan lanolate
- PEG-75 sorbitan lanolate*
- PEG-10 sorbitan laurate
- PEG-40 sorbitan laurate
- PEG-44 sorbitan laurate
- PEG-75 sorbitan laurate
- PEG-80 sorbitan laurate
- PEG-3 sorbitan oleate
- PEG-6 sorbitan oleate
- PEG-20 sorbitan oleate*
- PEG-80 sorbitan palmitate*
- PEG-40 sorbitan perisostearate*
- PEG-40 sorbitan peroleate
- PEG-4 sorbitan stearate*
- PEG-6 sorbitan stearate
- PEG-40 sorbitan stearate
- PEG-60 sorbitan stearate*
- PEG-30 sorbitan tetroleate
- PEG-40 sorbitan tetroleate
- PEG-60 sorbitan tetroleate
- PEG-60 sorbitan tetrastearate*
- PEG-4 sorbitan triisostearate*
- PEG-20 sorbitan triisostearate*
- PEG-160 sorbitan tristearate*
- sorbeth-2 beeswax*
- sorbeth-6 beeswax*
- sorbeth-8 beeswax*
- sorbeth-20 beeswax
- sorbeth-2 cocoate*
- sorbeth-2 hexacaprylate/caprate*
- sorbeth-12 hexacocoate*
- sorbeth-2 hexaisostearate*
- sorbeth-2 hexalaurate*
- sorbeth-2 hexaoleate*
- sorbeth-40 hexaoleate (PEG-40 sorbitol hexaoleate)*
- sorbeth-50 hexaoleate (PEG-50 sorbitol hexaoleate)*
- sorbeth-6 hexastearate*
- sorbeth-150 hexastearate*
- sorbeth-3 isostearate*
- sorbeth-6 laurate*
- sorbeth-2/oleate/dimer dilinoleate crosspolymer*
- sorbeth-20 pentaisostearate*
- sorbeth-30 pentaisostearate*
- sorbeth-40 pentaisostearate*
- sorbeth-50 pentaisostearate*
- sorbeth-40 pentaoleate*
- sorbeth-20 tetraisostearate*
- sorbeth-30 tetraisostearate
- sorbeth-40 tetraisostearate*
- sorbeth-450 tristearate*
- Sorbeth-50 tetraisostearate*
- sorbeth-4 tetraoleate
- sorbeth-6 tetraoleate
- sorbeth-30 tetraoleate
- sorbeth-40 tetraoleate
- sorbeth-60 tetraoleate
- sorbeth-30 tetroleate laurate (PEG-30 sorbitol tetroleate laurate)*
- sorbeth-60 tetrastearate (PEG-60 sorbitol tetrastearate)*
- sorbeth-3 tristearate*
- sorbeth-160 tristearate*
- sorbeth-450 tristearate*
- PEG-2 sorbitan trioleate*
- PEG-18 sorbitan trioleate
- PEG-3 sorbitan tristearate*
- PEG-12 hexacosanate*
- PEG-3 sorbitol hexaoleate*
- PEG-50 sorbitol hexaoleate*
- PEG-30 sorbitol hexaoleate*
- PEG-40 sorbitol hexaoleate*
- PEG-50 sorbitol hexaoleate*
- PEG-60 sorbitol hexaoleate*
- PEG-160 sorbitol tristearate*
- PEG-450 sorbitol tristearate*
- PEG-2 sorbitan trioleate*
- PEG-18 sorbitan trioleate
- PEG-3 sorbitan tristearate*
- PEG-12 hexacosanate*
- PEG-3 sorbitol hexaoleate*
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- PEG-160 sorbitol tristearate*
- PEG-450 sorbitol tristearate*
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- PEG-18 sorbitan trioleate
- PEG-3 sorbitan tristearate*
- PEG-12 hexacosanate*
- PEG-3 sorbitol hexaoleate*
- PEG-50 sorbitol hexaoleate*
- PEG-30 sorbitol hexaoleate*
- PEG-40 sorbitol hexaoleate*
- PEG-50 sorbitol hexaoleate*
- PEG-60 sorbitol hexaoleate*
- PEG-160 sorbitol tristearate*
- PEG-450 sorbitol tristearate*

*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.

This report combines the polysorbate ingredients from reports published in 1984, 2000, and 2001 and reflects a change in the Panel’s previous safe-as-used conclusion, with an additional restriction in the 2001 report. In the original safety assessment (2001) of sorbeth beeswax ingredients, the Panel recommended the qualification that cosmetic formulations containing the polyethylene glycol (PEG) moiety not be used on damaged skin. Since then, new data available in the re-review of PEG ingredients showed that PEGs, when used in cosmetics, would not cause renal damage when applied to damaged skin. Therefore, the qualification is removed from the conclusion for these, and all other PEG-containing cosmetic ingredients.

These ingredients mostly function as surfactants in cosmetics. Four of these ingredients have had name changes since their original safety assessments.

Tentative Safety Assessments

Tentative and tentative amended safety assessments will be posted on the CIR website at [www.cir-safety.org](http://www.cir-safety.org) on or before June 26, 2015. 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 July 31, 2015, or sooner if possible. These reports may be scheduled for review by the CIR Expert Panel at its September 21-22, 2015 meeting.
Citrus Fruit – Derived Ingredients

The Panel issued a tentative report for public comment with the conclusion that the 80 Citrus fruit-derived ingredients listed below are safe for use in cosmetic products when finished products, excluding rinse-off products, do not contain more than 0.0015% (15 ppm) 5-methoxypsoralen (5-MOP), and when formulated to be non-sensitizing and non-irritating.

citrus aurantifolia (lime)/citrus limon (lemon) fruit water*
citrus aurantifolia (lime) fruit* 
citrus aurantifolia (lime) fruit extract 
citrus aurantifolia (lime) fruit water* 
citrus aurantifolia (lime) juice

citrus aurantium amara (bitter orange) fruit extract

citrus aurantium amara (bitter orange) fruit/peel water* 
citrus aurantium bergamia (bergamot) fruit extract

citrus aurantium bergamia (bergamot) fruit water* 
citrus aurantium dulcis (orange) fruit extract

citrus aurantium dulcis (orange) fruit water* 
citrus aurantium dulcis (orange) juice

citrus aurantium sinensis (orange) fiber 
citrus clementina fruit extract* 
citrus clementina juice* 
citrus depressa fruit extract* 
citrus depressa fruit water* 
citrus glauca fruit extract 
citrus grandis (grapefruit) fruit extract

citrus grandis (grapefruit) fruit/peel water 
citrus grandis (grapefruit) fruit/peel water* 
citrus grandis (grapefruit) juice 
citrus grandis/paradisi fruit water* 
citrus hassaku fruit extract* 
citrus hassaku/natsudaidai fruit juice* 
citrus hassaku/natsudaidai fruit powder* 
citrus iyo fruit extract* 
citrus iyo fruit water* 
citrus jabara juice* 
citrus japonica fruit extract 
citrus junos fruit extract

citrus junos fruit juice* 
citrus junos fruit oil* 
citrus junos fruit powder* 
citrus junos fruit water* 
citrus limon (lemon) fruit extract

citrus limon (lemon) fruit oil* 
citrus limon (lemon) fruit powder* 
citrus limon (lemon) fruit 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.

While the available dermal irritation and sensitization data supported the safety of these Citrus fruit-derived ingredients at current use concentrations, constituents of these ingredients, such as the furocoumarin 5-MOP, can potentially cause phototoxicity. The Panel stated that standards, set by Research Institute for Fragrance Materials (RIFM) for use of these ingredients in fragrances, adequately protect against such adverse effects. The Panel also expressed concern that Citrus fruit-derived ingredients could be irritants and concluded that these botanicals must be formulated to be non-irritating.

RIFM confirmed that citrus aurantium bergamia (bergamot) fruit oil, which only has “fragrance” listed as a function in the Dictionary, is under review as a fragrance ingredient and is thus excluded from CIR’s purview for review. This ingredient was deleted from the report.

Nonoxynols

The Panel issued a tentative amended report for public comment with the conclusions that 19 nonoxynols, -9, -11, -10, -12, -13, -14, -15, -18, -20, -23, -25, -30, -35, -40, -44, -50, -70, -100, and -120, are safe in the present practices of use and concentration in cosmetics, and that 8 nonoxynols, -1, -2, -3, -4, -5, -6, -7, and -8, are safe as used in rinse-off products and safe at concentrations ≤ 5% in leave-on products. The 27 nonoxynols are listed below.

nonoxynol-1 nonoxynol-3 nonoxynol-5
nonoxynol-2 nonoxynol-4 nonoxynol-6
The Panel previously evaluated the safety of nonoxynols-2, -4, -8, -9, -10, -12, -14, -15, -30, -40, and -50 in cosmetics and issued a final report (published in 1983) with the conclusion these nonoxynols are safe as cosmetic ingredients in the present practices of concentration and use. The Panel reevaluated the safety of nonoxynols-2, -4, and -8 and evaluated the safety of nonoxynols-1, -3, -5, -6, and -7 in cosmetics for the first time, and issued a final report (published in 1999) with the conclusion that nonoxynols-1, -2, -3, -4, -5, -6, -7, and -8 are safe as used in rinse-off products and safe at concentrations ≤ 5% in leave-on products. This conclusion modified a previous conclusion for nonoxynols-2, -4, and -8, which had been considered safe as used in both rinse-off and leave-on products.

The Panel reopened the 1983 and 1999 final safety assessments to gain additional information on the basis for the European Union’s (EU) ≤ 0.1% limitation on the concentrations of nonylphenol ethoxylates (another name for nonoxynols) and nonylphenol in cosmetic and other industrial products, in light of the Panel’s previous conclusion that restricted the use of nonoxynols in leave-on products to concentrations < 5%. Restrictions in the European Union on the concentrations of nonylphenol and nonylphenol ethoxylates in industrial products is based on the premise that European water bodies are at risk from the persistence of the nonoxynols and their degradation products in the environment, and their potential to cause endocrine disruption in ecological species. The Panel determined that this is not an issue that is relevant for assessing the consumer safety of nonoxynols as used in cosmetic products.

### Polysaccharide Gums

The Panel issued a tentative report for public comment with the conclusion that the following 106 polysaccharide gums are safe in the present practices of use and concentration, and that the available data are insufficient for determining the safety of hydrolyzed carrageenan in cosmetic products. A total of 126 ingredients were reviewed in this report.

#### Linear Polysaccharides and Salts Thereof

<table>
<thead>
<tr>
<th>Linear – Modified</th>
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<tbody>
<tr>
<td>amylodextrin</td>
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<tr>
<td>hydrolyzed furcellaran</td>
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<td>maltodextrin</td>
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<tr>
<th>Branched Natural/Unmodified</th>
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<tbody>
<tr>
<td>amylpectin</td>
</tr>
<tr>
<td>aphanatheca sacrum polysaccharide</td>
</tr>
<tr>
<td>arabinoxylan</td>
</tr>
<tr>
<td>avena sativa (oat) starch cassia angustifolia seed polysaccharide</td>
</tr>
<tr>
<td>cichorium intybus (chicory) root oligosaccharides</td>
</tr>
<tr>
<td>triticum vulgare(wheat) starch</td>
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<table>
<thead>
<tr>
<th>Branched – Modified</th>
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</thead>
<tbody>
<tr>
<td>calcium starch</td>
</tr>
<tr>
<td>isododecenylsuccinate</td>
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<tr>
<td>octenylsuccinate</td>
</tr>
<tr>
<td>corn starch modified</td>
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<tr>
<td>dextrin</td>
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<tr>
<td>dextrin behenate</td>
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<tr>
<td>dextrin isostearate</td>
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<td>dextrin laurate</td>
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<td>dextrin myristate</td>
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<td>dextrin palmitate</td>
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<td>dextrin</td>
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<tr>
<td>palmitate/ethylhexanoate</td>
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<tr>
<td>dextrin stearate</td>
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<tr>
<td>glyceryl alginate</td>
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<td>glyceryl dimaltodextrin</td>
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</table>

The Panel reopened the 1983 and 1999 final safety assessments to gain additional information on the basis for the European Union’s (EU) ≤ 0.1% limitation on the concentrations of nonylphenol ethoxylates (another name for nonoxynols) and nonylphenol in cosmetic and other industrial products, in light of the Panel’s previous conclusion that restricted the use of nonoxynols in leave-on products to concentrations ≤ 5%. Restrictions in the European Union on the concentrations of nonylphenol and nonylphenol ethoxylates in industrial products is based on the premise that European water bodies are at risk from the persistence of the nonoxynols and their degradation products in the environment, and their potential to cause endocrine disruption in ecological species. The Panel determined that this is not an issue that is relevant for assessing the consumer safety of nonoxynols as used in cosmetic products.
**alginate**

**starch acetate/adipate**

**starch diethylaminoethyl ether**

**TEA-dextrin octenylsuccinate**

**starch hydroxypropyltrimonium chloride**

**starch laurate**

**undecylenoyl inulin**

**starch tallowate**

**stearoyl inulin**

**tapioca starch crosspolymer**

**Cyclic**

**cyclodextrin**

**cyclotetraglucose**

**Cyclic – Modified**

**hydroxyethyl cyclodextrin**

**hydroxypropyl cyclodextrin**

**cyclodextrin hydroxypropyltrimonium chloride**

**cyclodextrin laurate**

**methyl cyclodextrin**

**Unknown Structural Configuration**

**algae exopolysaccharides**

**cassia angustifolia seed polysaccharide**

**prunus persica (peach) gum**

**Unknown Structural Configuration – Modified**

**hydrogenated potato starch**

**hydrogenated starch hydrolysate**

**hydrolyzed corn starch hydroxyethyl ether**

**hydrolyzed corn starch octenylsuccinate**

**The Panel was concerned about the absence of adequate information to distinguish between the cosmetic ingredient hydrolyzed carrageenan and degraded carrageenan (poligeenan). A study suggested the induction of colon tumors in rats that received degraded carrageenan (poligeenan) in the diet. Although composition data on hydrolyzed carrageenan and degraded carrageenan (poligeenan) were not available, the Panel noted that, given the no-observed-effect level (NOEL) for colon carcinogenicity in the oral studies and the maximum use concentration of polysaccharide gums in lipstick products, the burden to the colon that would result from the incidental ingestion of lipstick would be well below the NOEL.**

**Additional information was received on a previous report that indicated the inhalation of konjac flour induced respiratory sensitization in test animals. Additional research suggested that the purified antigen AG40D-2 (acidic protein) was responsible for the respiratory sensitization observed, and that this effect was not attributed to glucomannan. Thus, the Panel’s concerns relating to the respiratory sensitization potential of glucomannan were addressed.**

**The Panel expressed concern about pesticide residues and heavy metals that may be present in botanical ingredients. They stressed that the cosmetics industry should continue to use current good manufacturing practices (cGMPs) to limit impurities. They agreed that the same concern and suggestion are applicable to alkylating and other agents (e.g., haloethylaminopropionic acid; 3-(dodecenyl)-2,5-furandione; and 2,3-epoxypropyltrimethylammonium chloride) that are used to modify polysaccharide gums.**

**Soy Proteins and Peptides**

The Panel issued a tentative safety assessment with the conclusion that the 6 soy-based ingredients listed below are safe in cosmetics in the present practices of use and concentration:

**glycine max (soybean) polypeptide**

**glycine soja (soybean) peptide**

**glycine soja (soybean) protein**

**hydrolyzed soy protein**

**hydrolyzed soy protein extract**

**hydrolyzed soymilk protein**

*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.*

**Trialkyl Trimellitates**

The Panel issued a tentative report for public comment with the conclusion that the following 5 trialkyl trimellitates are safe as used in cosmetics at the present practices of use and concentration when formulated to be non-irritating:

**tridecyl trimellitate**
tricaprylyl/capryl trimellitate*
triethylhexyl trimellitate
triisodecyl trimellitate
triisotridecyl trimellitate

*Not reported to be in current use. Were this ingredient 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 discussed the observation that triethylhexyl trimellitate exhibited estrogenic activity in an in vitro test using human osteoblastic (US-O2) reporter gene cell lines for ERα and ERβ. However, trialkyl trimellitates are not expected to be absorbed through the skin, thus the Panel was not concerned with risks imposed by this observation.

The Panel noted studies suggesting the induction of peroxisome proliferation by triethylhexyl trimellitate, however it appeared only to have a weak effect on peroxisome proliferation. They further stated that even if there was an effect, peroxisome proliferation is not believed to pose the risk of inducing hepatocarcinogenesis in humans because humans do not react to peroxisome proliferators in the same manner as rodents.

Although no carcinogenicity data were available, negative genotoxicity data on tricaprylyl/capryl trimellitate and triethylhexyl trimellitate, the lack of structural alerts for carcinogenicity, and expected low dermal penetration, led the Panel to conclude that carcinogenicity would not be a concern with cosmetic use of these ingredients.

The Panel recognized that there were little toxicity data available for the branched ingredient triisodecyl trimellitate. They concluded that despite the absence of this information, there is little concern about the safety of this ingredient as used in cosmetics. However, if data are available on triisodecyl trimellitate, they could serve to strengthen the safety evaluation.

**Insufficient Data Announcement**

*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 July 31, 2015, or sooner if possible. These reports are scheduled for review by the CIR Expert Panel at its September 21-22, 2015 meeting.*

**Alkonium Clays**

The Panel issued an Insufficient Data Announcement for the 8 alkonium clays listed below. These ingredients are the products of the reactions of an ammonium salt with a smectite clay. These ingredients are reported to function as dispersing agents-nonsurfactant, emulsion stabilizers, and viscosity increasing agents-nonaqueous.

<table>
<thead>
<tr>
<th>Ingredient</th>
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<tbody>
<tr>
<td>hydrogenated tallowalkonium bentonite</td>
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<tr>
<td>quaternium-18/benzalkonium bentonite</td>
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<tr>
<td>quaternium-90 bentonite</td>
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<td>benzalkonium sepiolite</td>
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<tr>
<td>quaternium-90 sepiolite</td>
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</table>

The data requested by the Panel are:
- Particle size distributions relevant for assessing potential inhalation exposures
- Percent (by weight) alkonium cation in these ingredients and the percent (by weight) releasable/exchangeable in solution
- Inhalation data at concentration of use (2.2% in powders and 3.2% in sprays)
- Ocular irritation at concentration of use, if available

**Pyrus malus-derived Ingredients**

*Pyrus malus* and *Malus domestica* are two genus and species names for apple. The Panel agreed that the available data are sufficient for evaluating the safety of the following 19 apple-derived ingredients in cosmetics, the ingredient source being either the fruit or seed.

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<thead>
<tr>
<th>Ingredient</th>
</tr>
</thead>
<tbody>
<tr>
<td>pyrus malus (apple) carpel powder</td>
</tr>
<tr>
<td>pyrus malus (apple) fiber</td>
</tr>
<tr>
<td>pyrus malus (apple) fruit extract</td>
</tr>
<tr>
<td>pyrus malus (apple) fruit</td>
</tr>
<tr>
<td>pyrus malus (apple) fruit water</td>
</tr>
<tr>
<td>pyrus malus (apple) juice</td>
</tr>
<tr>
<td>pyrus malus (apple) pectin extract</td>
</tr>
<tr>
<td>pyrus malus (apple) peel extract</td>
</tr>
<tr>
<td>pyrus malus (apple) peel powder</td>
</tr>
<tr>
<td>pyrus malus (apple) peel wax</td>
</tr>
<tr>
<td>pyrus malus (apple) pulp extract</td>
</tr>
<tr>
<td>pyrus malus (apple) seed extract</td>
</tr>
<tr>
<td>pyrus malus (apple) seed oil</td>
</tr>
<tr>
<td>malus domestica (apple) fiber</td>
</tr>
<tr>
<td>malus domestica (apple) fruit extract</td>
</tr>
<tr>
<td>malus domestica (apple) fruit water</td>
</tr>
<tr>
<td>malus domestica (apple) fruit cell culture extract</td>
</tr>
<tr>
<td>malus domestica (apple) juice</td>
</tr>
<tr>
<td>malus domestica (apple) seed oil</td>
</tr>
</tbody>
</table>

However, the Panel issued an insufficient data announcement on the following 9 apple-derived ingredients:
The data that are needed to evaluate the safety of these 12 ingredients are:

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

**Silk Proteins**

The safety of 10 silk protein ingredients in cosmetics is reviewed in this safety assessment. The Panel agreed that the available data are sufficient for evaluating the safety of the following 8 silk protein ingredients.

<table>
<thead>
<tr>
<th>Ingredient</th>
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</thead>
<tbody>
<tr>
<td>fibroin</td>
</tr>
<tr>
<td>hydrolyzed fibroin</td>
</tr>
<tr>
<td>hydrolyzed sericin</td>
</tr>
<tr>
<td>hydrolyzed silk</td>
</tr>
<tr>
<td>sericin</td>
</tr>
<tr>
<td>silk</td>
</tr>
<tr>
<td>silk extract</td>
</tr>
<tr>
<td>silk powder</td>
</tr>
</tbody>
</table>

However, the Panel issued an insufficient data announcement on two silk protein ingredients, MEA-Hydrolyzed Silk and Silkworm Cocoon Extract:

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

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

**Re-review Summaries**

The Panel approved the summaries of their actions at the March meeting to not reopen the safety assessments of bisabolol and isostearamidopropyl morpholine lactate. The Panel also reiterated the CIR Procedures, that call for a change in classification of this ingredient from insufficient to “Use Not Supported by the Data and Information Submitted to the CIR”, if after 2 years, the data requests are not fulfilled and this ingredient continues to have reported use in leave-on formulations according to the VCRP.

**135th Meeting Notes**

**Director’s Report**

Dr. Gill discussed 2 projects that CIR is initiating this month. The first project focuses on the development of an electronic document-management and tracking system with a goal of enhancing the project management and workflow efficiencies in CIR. It is the first step in building an information management framework that combines authoring capability, bibliography and document management, workflow of records, and the storage and retrieval of safety assessments and related files. The goal of the second initiative is to enhance the scientific and technical CIR capability of applying computational methods in the ingredient safety assessment process. Efforts this year will focus on evaluating the available computational methods for filling data gaps, including read-across of in vivo data or predictions such as QSAR results (e.g., chemical similarity, analog quality, in vivo data quality). Additionally, this project includes the development of a schema and “ground floor” electronic data system that CIR anticipates will lead to a full CIR toxicity and risk assessment database.

Dr. Gill mentioned that a presentation from Industry is scheduled for the September 21-22, Panel meeting. The Silicones Environmental, Health and Safety Center have asked to provide a brief chemistry overview on polysilicones.

Dr. Gill congratulated the Panel Chair, Dr. Wilma Bergfeld, for her recent honor. In early June, at the 23rd World Congress of Dermatology meeting in Vancouver, Galderma Pharma recognized Dr. Bergfeld as one of the top 4 women dermatologist leaders across the world. (Dr. Bergfeld is also the founding President of the Women’s Dermatology Society, which is over 40 years old.) In recognition of this outstanding accomplishment, Galderma honored the 4 international women dermatologist in a bigger than life mural which was painted on-site during the meeting. The mural will hang in the lobby of Galderma Pharma’s corporate office in New York.

**Briefing on Plant Cell Cultures as a Source for Cosmetic ingredients**

Roberto Dal Toso, Ph.D., is the co-founder and R&D manager of the Instituto di Richerch Biotechnologiche (I.R.B.), SpA, currently known as Croda-Sederma. At the request of the Industry, Dr. Dal Toso delivered a presentation to the Panel on the development and use of plant cell cultures as sources of ingredients for cosmetics and foods, among other products.
Dr. Dal Toso explained that meristematic tissues enable the growth of plants. These tissues are composed of rapidly dividing, undifferentiated and incompletely differentiated stem cells (i.e., meristem cells). Meristem cells are found predominantly in the apical shoot and root tips, as well as in cylinder-shaped cambial meristem tissues that are responsible for the lateral growth of plants and in seeds. Meristem cells can be harvested and grown as calluses on solid culture media. Each callus is a blend of numerous undifferentiated cells. Calluses can also be obtained from differentiated (“adult”) cells of a plant through dedifferentiation, which produces cells exhibiting the characteristics of meristem cells.

Dr. Dal Toso explained that producing plant cell cultures as a source of cosmetic ingredients begins by selecting, sterilizing the surfaces of, and explanting plant parts from which to grow calluses on relatively simple solid nutrient media. Establishing a stable culture takes about two years. Once established, the culture can be maintained as a stable cell line and an unlimited source of ingredients for many years. These cultures are not different genetically from the plants from which they are derived and, thus, are not genetically modified.

The cultures developed in this manner have no contact with the environment outside of the laboratory, and therefore exhibit no variations in composition from differences in geographical, climatic, or seasonal conditions and harvesting methods, and need no protection from pesticides or other substances typically used in the cultivation of plants in the field. These highly controlled conditions also help to limit the variations in constituents that would be expected from the natural biological cycles of plants growing in the field, and ensures the absence of contamination from soil microorganisms, aflatoxins, heavy metals, and other pollutants in the ingredients derived from the cultures.

Dr. Dal Toso presented analytical data showing that the constituents of *Centella asiatica* meristem cells were comparable to that of a “classical” *Centella asiatica* extract identified as a cosmetic ingredient. He also presented data from tests of a commercial *Centella asiatica* meristem cell culture product indicating the lack of irritation, mutagenicity, and phototoxicity *in vitro*, and the absence of irritation in a human repeat insult patch test.

**Reports Tabled - none**

**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)

  - alkyl taurate amides and salts
  - HDI polymers
  - inorganic hydroxides
  - trimellitic anhydride copolymers

  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 September 21-22, 2015.

- These literature reviews are currently under development

  *Ginkgo biloba*-derived ingredients
  - keratin proteins
  - *Helianthus annuus* (Sunflower)-derived ingredients
  - phosphoric acid, its simple salts, & the metaphosphates
  - polyglyceryl fatty acid esters
  - simple carbonate salts

- Re-reviews scheduled for the next Panel meeting

  - glyceryl stearate

**Draft 2016 Ingredient Review Priorities**

The following 2016 Priority list was approved by the CIR Expert Panel. There are 18 ingredient/ingredient groups on the list. However, it is likely that not all of those listed will be chosen for work in 2016.

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Number of formulations containing ingredient</th>
</tr>
</thead>
<tbody>
<tr>
<td>propanediol</td>
<td>548</td>
</tr>
<tr>
<td>linoleic acid</td>
<td>532</td>
</tr>
<tr>
<td>hydroxyethyl acrylate/sodium</td>
<td>446</td>
</tr>
<tr>
<td>acryloxydimethyl taurate copolymer</td>
<td>421</td>
</tr>
<tr>
<td>ammonium acryloxydimethyltaurate/ vp copolymer</td>
<td>426</td>
</tr>
<tr>
<td>hydrofluorocarbon 152a</td>
<td>409</td>
</tr>
</tbody>
</table>
These 2016 CIR priorities are based on those ingredients listed in the 2015 VCRP data that have not been reviewed by CIR and have the largest number of uses, or have been specifically requested by stakeholders. Some ingredients are excluded from review by the CIR, as discussed in the CIR Procedures. This list only names the lead ingredients. Families of ingredients may be reviewed, as appropriate (proposed ingredient families are posted on the CIR website). Interested parties are encouraged to submit data pertinent to these ingredients to the CIR for use in the development of the Scientific Literature Review. Although the specific data needs vary for each safety assessment, the following are typical data that the Panel reviews for each safety assessment.

• chemistry, impurities, and method of manufacture
• toxicokinetics data, specifically dermal absorption and/or penetration
• repeated-dose toxicity data
• inhalation toxicity data, if the ingredient is used in a product that can be incidentally inhaled
• reproductive/developmental toxicity data
• genotoxicity data; and if positive, carcinogenicity data may be needed
• dermal irritation and sensitization data

For the review of botanical ingredients, the additional data needed include: species, plant part, extraction method, solvent, and data on component chemical characterization. It is important that these data are specific to the cosmetic ingredient(s).

Next CIR Expert Panel Meeting

Monday and Tuesday, September 21-22, 2015, at The Hilton – DoubleTree Hotel, Washington, DC 20005 --- Please contact Carla Jackson (jacksonc@cir-safety.org) at CIR before the meeting if you plan to attend.