
Announcement

Cosmetic Ingredient Review Expert Panel 137th Meeting (December 14-15, 2015) - Findings

December 18, 2015

- **Final Safety Assessments**

- Alkyl Taurate Amides and Taurate Salts – 20 ingredients
- Citrus Fruit-Derived Ingredients – 80 ingredients
- Inorganic Hydroxides – 4 ingredients
- Monoglyceryl Monoesters – 44 ingredients
- Nonoxynols – 27 ingredients
- Silk Proteins – 10 ingredients

- **Tentative Safety Assessments**

- Alkonium Clays – 8 ingredients
- Apple-Derived Ingredients – 26 ingredients
- Hexamethylene Diisocyanate (HDI) Polymers – 19 ingredients
- 1-Hydroxyethyl-4,5-diamino Pyrazole Sulfate – 1 ingredient
- Polymerized Tetramethylcyclotetrasiloxane – 3 ingredients
- Trimellitic Anhydride Copolymers – 6 ingredients

- **Insufficient Data Announcement**

- Citrus Flower- and Leaf-Derived Ingredients – 32 ingredients
- Citrus Peel-derived ingredients – 47 ingredients
- Citrus Plant- and Seed-Derived Ingredients – 33 ingredients
- *Helianthus annuus* (Sunflower)-Derived Ingredients – 13 ingredients

- **Re-Reviews - none**

- **137th Meeting Notes**

- Director's Report
 - Other Items
- Scientific Literature Reviews posted on the CIR website
- Scientific Literature Reviews under development
- Re-reviews for the next Panel meeting
- Next Expert Panel Meeting – Thursday and Friday, March 31 – April 1, 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 Unpublished data cited as references in CIR safety assessments are available for review.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.

Alkyl Taurate Amides and Taurate Salts

The following 20 alkyl taurate amides and taurate salts were found safe as used in cosmetics when formulated to be non-irritating:

potassium taurate*	sodium <i>n</i> -isostearoyl methyltaurate*
sodium methyltaurate	sodium lauroyl taurate
sodium taurate*	sodium methyl lauroyl taurate
calcium lauroyl taurate	sodium methyl myristoyl taurate
magnesium methyl cocoyl taurate*	sodium methyl oleoyl taurate
potassium cocoyl taurate*	sodium methyl palmitoyl taurate
potassium methyl cocoyl taurate	sodium methyl stearoyl taurate
sodium caproyl methyltaurate*	sodium methyltaurate isopalmitamide*
sodium cocoyl taurate	sodium methyltaurine cocoyl methyltaurate
sodium methyl cocoyl taurate	sodium taurine cocoyl methyltaurate*

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

The Panel noted that the animal sensitization data were sufficient to demonstrate the safety of these ingredients. Although there were no impurity data and these amides and salts may be absorbed through the skin, the available systemic toxicity studies raised no concerns and the negative genotoxicity assays were sufficient to address any concerns about the lack of carcinogenicity data.

Sodium methyl cocoyl taurate had the highest reported number of uses; it is used in 339 formulations, most of which are in rinse-off products. Sodium methyl oleoyl taurate had the highest reported maximum use concentration; 28% in bath products. This was followed by sodium cocoyl taurate with a maximum concentration of use of 21.5% in rinse-off personal cleanliness products. Calcium lauroyl taurate and sodium methyl cocoyl taurate are used at up to 11% (highest concentration in a leave-on product) and 13%, respectively. All the other ingredients with reported concentrations of use are used at 6% or less.

Citrus Fruit-Derived Ingredients

The following 80 *Citrus* fruit-derived ingredients are safe for use in rinse-off and leave-on cosmetic products when formulated to be non-sensitizing and non-irritating, provided that leave-on products do not contain more than 0.0015% (15 ppm) 5-methoxypsoralen (5-MOP).

citrus aurantifolia (lime)/citrus limon (lemon) fruit water*	citrus japonica fruit extract
citrus aurantifolia (lime) fruit*	citrus junos fruit extract
citrus aurantifolia (lime) fruit extract	citrus junos fruit juice*
citrus aurantifolia (lime) fruit water*	citrus junos fruit oil*
citrus aurantifolia (lime) juice	citrus junos fruit powder*
citrus aurantium amara (bitter orange) fruit extract	citrus junos fruit water*
citrus aurantium amara (bitter orange) fruit juice extract*	citrus limon (lemon) fruit extract
citrus aurantium bergamia (bergamot) fruit extract	citrus limon (lemon) fruit oil*
citrus aurantium bergamia (bergamot) fruit water*	citrus limon (lemon) fruit powder*
citrus aurantium dulcis (orange) fruit extract	citrus limon (lemon) fruit water
citrus aurantium dulcis (orange) fruit powder*	citrus limon (lemon) juice
citrus aurantium dulcis (orange) fruit water	citrus limon (lemon) juice extract
citrus aurantium dulcis (orange) juice	citrus limon (lemon) juice powder*
citrus aurantium sinensis (orange) fiber	citrus madurensis fruit extract
citrus clementina fruit extract*	citrus madurensis fruit juice*
citrus clementina juice*	citrus medica vulgaris fruit extract
citrus depressa fruit extract*	citrus nobilis (mandarin orange) fruit extract
citrus depressa fruit water*	citrus nobilis (mandarin orange) fruit juice
citrus glauca fruit extract	citrus paradisi (grapefruit) fruit extract
citrus grandis (grapefruit) fruit extract	citrus paradisi (grapefruit) fruit water*
citrus grandis (grapefruit) fruit/peel water	citrus paradisi (grapefruit) juice*
citrus grandis (grapefruit) fruit water	citrus reticulata (tangerine) fruit*
citrus grandis (grapefruit) juice	citrus reticulata (tangerine) fruit extract
citrus grandis/paradisi fruit water*	citrus reticulata (tangerine) fruit water*
citrus hassaku fruit extract*	citrus shunkokan fruit extract*
citrus hassaku/natsudaidai fruit juice*	citrus sinensis (orange) fruit extract
citrus hassaku/natsudaidai fruit powder*	citrus sinensis (orange) fruit water
citrus iyo fruit extract*	citrus sphaerocarpa fruit juice*
citrus iyo fruit water*	citrus sudachi fruit extract*
citrus jabara juice*	citrus sudachi fruit juice*

citrus tachibana/reticulata fruit juice*
citrus tamurana fruit extract*
citrus tangelo fruit juice*
citrus tangelo fruit powder*
citrus tangerina (tangerine) fruit*
citrus tangerina (tangerine) fruit water*
citrus tankan fruit extract*
citrus tankan fruit water*
citrus unshiu/citrus reticulata/citrus iyo fruit water*
citrus unshiu fruit extract*

citrus unshiu fruit juice*
citrus unshiu fruit juice ferment extract filtrate
citrus unshiu fruit oil*
citrus unshiu fruit powder*
citrus unshiu fruit water*
citrus unshiu/sinensis/reticulata fruit extract*
defatted citrus unshiu fruit*
hydrolyzed citrus aurantium dulcis fruit extract
microcitrus australasica fruit extract*
microcitrus australis fruit 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 International Fragrance Association (IFRA) standard for 7-methoxycoumarin was removed from mention in this safety assessment. Although the IFRA standard was issued for all natural ingredients, there are no data to indicate that 7-methoxycoumarin is a constituent of *Citrus* fruit-derived ingredients.

The available dermal irritation and sensitization data supported the safety of these *Citrus* fruit-derived ingredients; however they have the potential to cause phototoxicity. The Panel considered the standards set by Research Institute for Fragrance Materials (RIFM) to be adequate to prevent such adverse effects. Additionally, the Panel concluded that these botanical ingredients must be formulated to be non-irritating because *Citrus* fruit-derived ingredients are potential irritants.

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

Inorganic Hydroxides

The 4 inorganic hydroxides listed below are safe in hair straighteners and depilatories under conditions of recommended use; users should minimize skin contact. These ingredients are safe for all other present practices of use and concentration described in this safety assessment when formulated to be nonirritating.

calcium hydroxide
magnesium hydroxide

potassium hydroxide
sodium hydroxide

The Panel recognized that while these ingredients may be dermal and/or ocular irritants, when used as pH adjusters in cosmetic formulations, most of the alkalinity will be neutralized. Because the concentration of the inorganic hydroxides used is dependent on the acid content of the formulation, the concentration of free inorganic hydroxide is expected to be low, and systemic toxicity is not expected to be a concern. The safety of inorganic hydroxides as pH adjusters should not be based on the concentration of use, but on the amount of free inorganic hydroxide that remains after neutralizing the formulation.

These ingredients also have reported functions as absorbents (magnesium hydroxide) and denaturants (sodium hydroxide). The Panel discussed the use of inorganic hydroxides for the purpose of these functions and had no concerns regarding their safety as long as these ingredients are formulated to be nonirritating.

The Panel discussed the use of inorganic hydroxides as depilatories and hair straighteners at very high pHs and concentrations. If these hydroxides are used in hair care products, a limitation on use concentrations and adequate instructions to users to avoid skin contact of the hands (such as by wearing gloves) and to minimize skin exposure (by limiting the frequency of product use) would be adequate to assure that irritation is not a concern. Without adequate skin protection, the Panel noted that repeated applications of hair straighteners containing inorganic hydroxides by hairdressers to multiple clients should be avoided. In addition, users should avoid prolonged skin exposures (both hands and scalp). The Panel recognizes that nearly all methods of hair removal may cause some irritation. However, in the experience of the Panel, clinically significant adverse reactions to these ingredients in depilatories are not commonly seen. This suggests that current products are formulated to be practically nonirritating under conditions of recommended use.

The Panel addressed the comments submitted by Women's Voices for the Earth and Black Women for Wellness regarding irritation and other adverse events caused by the use of depilatories and hair straighteners. The Panel discussed the need to use inorganic hydroxides at concentrations yielding high pHs in these types of products for them to function as desired, and restated that users should follow the manufacturer's instructions for proper use, especially if the products are to be used on children. Additionally, after reviewing of adverse events reported in the literature for depilatories and hair straighteners, the Panel noted that these affects may be due to ingredients other than the inorganic hydroxides in these formulations.

Monoglyceryl Monoesters

The Panel issued a final amended report with the conclusion that the following 44 monoglyceryl monoesters are safe as used in cosmetics:

glyceryl acetate*
glyceryl adipate*
glyceryl arachidate*
glyceryl behenate
glyceryl caprate
glyceryl caprylate
glyceryl caprylate/caprate
glyceryl citrate/lactate/linoleate/oleate
glyceryl cocoate

glyceryl cocoate/citrate/lactate*
glyceryl erucate*
glyceryl ethylhexanoate*
glyceryl ethylhexanoate/stearate/adipate
glyceryl heptanoate*
glyceryl hydrogenated rapeseedate*
glyceryl hydrogenated rosinatate
glyceryl hydrogenated soyate*
glyceryl hydroxystearate

glyceryl isopalmitate*
 glyceryl isostearate
 glyceryl isotridecanoate/stearate/ adipate
 glyceryl lanolate
 glyceryl laurate
 glyceryl laurate SE*
 glyceryl laurate/oleate*
 glyceryl linoleate
 glyceryl linolenate
 glyceryl montanate*
 glyceryl oleate
 glyceryl oleate SE*
 glyceryl oleate/elaidate

glyceryl olivate*
 glyceryl palmitate
 glyceryl palmitate/stearate*
 glyceryl palmitoleate*
 glyceryl pentadecanoate*
 glyceryl ricinoleate
 glyceryl ricinoleate SE
 glyceryl rosinate
 glyceryl stearate
 glyceryl stearate SE
 glyceryl stearate/malate
 glyceryl tallowate*
 glyceryl undecylenate

*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.

All but 8 of the ingredients included in this report have been previously reviewed by the Panel. In 1982, the Panel concluded that glyceryl stearate and glyceryl stearate SE are safe for topical application to humans; this conclusion will supersede the 1982 conclusion. The remaining previously reviewed ingredients were found safe as used in the original reviews; those conclusions were reaffirmed for these 34 ingredients.

For many of the ingredients included in the report, the frequency of use has increased since the Panel's original review, but the concentration of use has not. However, there are a few ingredients for which the concentration of use has increased; these increased concentrations were not a concern to the Panel.

Nonoxynols

The Panel issued a final amended report with the conclusion that the following 27 nonoxynols are safe in the present practices of use and concentration in cosmetics, when formulated to be non-irritating:

nonoxynol-1	nonoxynol-10	nonoxynol-25*
nonoxynol-2	nonoxynol-11*	nonoxynol-30
nonoxynol-3*	nonoxynol-12	nonoxynol-35*
nonoxynol-4	nonoxynol-13*	nonoxynol-40*
nonoxynol-5	nonoxynol-14	nonoxynol-44*
nonoxynol-6	nonoxynol-15	nonoxynol-50*
nonoxynol-7*	nonoxynol-18*	nonoxynol-70*
nonoxynol-8*	nonoxynol-20*	nonoxynol-100*
nonoxynol-9	nonoxynol-23	nonoxynol-120*

*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 previously issued a final report (published in 1983) with the conclusion that nonoxynols-2, -4, -8, -9, -10, -12, -14, -15, -30, -40, and -50 are safe as cosmetic ingredients in the present practices of concentration and use. A final report (published in 1999) that 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, was issued 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. The 5% concentration limit was based on the potential for skin irritation. 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.

At the September 2015 meeting, the Panel discussed the 5% concentration limit in response to correspondence received about a cosmetic product (cosmetic feminine wash – intended for use on the vaginal area) containing a then unknown concentration of nonoxynol-9 that is being marketed in the United States. The Panel removed the 5% concentration limit and issued a revised conclusion that cosmetic products containing nonoxynols should be formulated to be non-irritating. Subsequently, the manufacturer of the feminine wash informed the Panel that the product contains 3% nonoxynol-9, and that nonoxynol-9 would be removed from this product. Although the review of nonoxynol-9 as a spermicidal ingredient (non-cosmetic use) is not within the Panel's purview, data indicating that the nonoxynol-9 in spermicidal products can cause mucous membrane irritation in animals and in humans were considered in the Panel's safety evaluation. All of the spermicidal products can cause mucous membrane irritation. The Panel also reviewed an FDA over-the-counter drug (OTC) monograph on nonoxynol-9, in the search for effective use concentrations in spermicidal gels and information on the likely concentration-response relationship between nonoxynol-9 concentrations and spermicidal activity. This information was not found in the monograph.

In response to the Panel's "safe when formulated to be non-irritating conclusion," Women's Voices for the Earth (WVE) submitted a letter to the Panel expressing concern about vaginal mucous membrane irritation that could result from use of the cosmetic feminine wash containing nonoxynol-9. Specifically, WVE requested that the Panel modify their conclusion, considering the absence of any proven no-effect-level for nonoxynol-9-induced vaginal irritation. The Panel acknowledged that nonoxynol-9 may be irritating to mucous membranes depending on the formulation and the intended use of products containing this ingredient. After lengthy discussion, the Panel confirmed their earlier conclusion that the nonoxynols are safe in the present practices of use and concentration in cosmetic products when formulated to be non-irritating.

Silk Protein Ingredients

The Panel issued a final report with the conclusion that the following 8 silk protein ingredients are safe in the present practices of use and concentration in cosmetics as described in this safety assessment.

fibroin*	sericin
hydrolyzed fibroin	silk
hydrolyzed sericin	silk extract
hydrolyzed silk	silk powder

The Panel also concluded that the available data are insufficient for evaluating the safety of 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; if absorbed, genotoxicity and reproductive and developmental toxicity may be needed
- Skin irritation and sensitization

*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 a study in which an 8% sericin cream applied to the skin of patients with renal disease caused depigmentation, which is a non-cosmetic effect (drug effect). Although drug effects are not within the Panel's purview, they noted that an effect on cutaneous pigmentation would not be expected at the use concentrations of silk protein ingredients in cosmetic products.

Studies on patients inhalationally exposed to silk waste, which is distinct from the silk protein ingredients that are being evaluated in this safety assessment, showed an association between asthma and dermal allergies to silk in children in China. The Panel determined that the results of these studies do not support a cause-and-effect relationship between the silk protein ingredients in this safety assessment and the development of asthma. However, because some of the silk protein ingredients are used in products that may be inhaled, a statement addressing inhalation exposure and the absence of respiratory effects or systemic effects is included in the report. Additionally, because of the available heavy metal impurities data on hydrolyzed silk and the potential for indirect contamination of host plants during silkworm cultivation, which may result from the use of pesticides, concern about the presence of pesticides and heavy metals in silk protein ingredients are also addressed in the report.

Tentative Safety Assessments

*Tentative and revised tentative safety assessments will be posted on the CIR website at www.cir-safety.org on or before **January 6, 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 **February 8, 2016, or sooner if possible**. These reports may be scheduled for review by the CIR Expert Panel at its **March 31-April 1, 2016** meeting.*

Alkonium Clays

The Panel issued a revised tentative report for public comment with the conclusion that these 8 alkonium clays listed below are safe 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. These ingredients are reported to function as dispersing agents-nonsurfactant, emulsion stabilizers, and viscosity increasing agents-nonaqueous.

Stearalkonium bentonite had the most reported uses at 423, including 420 leave-on uses and 3 rinse-off uses; it was reported to be used up to 6.5% in nail polish and enamel, 2.4% in lipstick, and 2.5% in eye shadow. Quaternium-90 bentonite was reported to be used in 64 leave-on products; it was reported to be used up to 6.1% in mascara and up to 6.1% in lipstick. There were no reported uses in powders.

Apple-derived Ingredients

The Panel issued a tentative report for public comment 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 genus and species 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) leaf extract*

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

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; if absorbed, genotoxicity and reproductive and developmental toxicity may be needed

Pyrus malus (apple) seed oil and malus domestica (apple) seed oil will be removed from the current safety assessment because the safety of the pyrus malus (apple) seed oil in cosmetics was evaluated in the CIR safety assessment on plant-derived fatty acid oils, and it was confirmed that both names refer to the same ingredient. The CIR safety assessment on plant-derived fatty acid oils will be revised to indicate that the “safe as used” conclusion on pyrus malus (apple) seed oil is also applicable to malus domestica (apple) seed oil.

The Panel noted that the composition of ingredients derived from different cultivars should be similar to the composition of ingredients reviewed in this safety assessment.

The Panel noted that phloridzin, a constituent of apple root bark powder and apple leaf extract, stimulated melanogenesis *in vitro*. They further stated that an effect on cutaneous pigmentation would not be expected at ingredient use concentrations of apple-derived ingredients in cosmetic products. However, as a precaution, manufacturers should be aware of this effect and were advised that formulations using ingredients containing phloridzin should not have a stimulatory effect on melanogenesis when applied to the skin.

Hexamethylene Diisocyanate (HDI) Polymers

The Panel issued a tentative report for public comment with the conclusion that the following 7 hexamethylene diisocyanate (HDI) polymers are safe as used:

HDI/trimethylol hexyllactone crosspolymer
bis-C16-20 isoalkoxy TMHDI/PEG-90 copolymer
bis-lauryl cocaminopropylamine/HDI/PEG-100 copolymer*
HDI/Di-C12-14 alkyl tartrate/hydrogenated dilinoleyl alcohol copolymer
methoxy PEG-17/methoxy PEG-11/HDI crosspolymer
PEG-240/HDI copolymer bis-decyltetradeceth-20 ether
steareth-100/PEG-136/HDI copolymer

The Panel concluded that the data on the following 12 HDI polymers are insufficient to determine safety:

bis-hydroxyethyl acrylate poly(1,4-butanediol)-9/TMHDI copolymer*
bis-isostearyl 1,4-butanediol/HDI/hydrogenated dimer dilinoleyl alcohol copolymer*
bis-methoxy PEG-10 dimethyl MEA/HDI/bis-PEG-10 dimethicone copolymer*
1,4-butanediol/succinic acid/adipic acid/HDI copolymer*
cholesterol/HDI/pullulan copolymer*
decyl HDI/PEG-180 crosspolymer*
diethylene glycol/DMAP acrylamide/ PEG-180/HDI copolymer
HDI/PEI-45/SMDI crosspolymer*
HDI/PPG/polycaprolactone crosspolymer
methoxy PEG-17/methoxy PEG-11/HDI isocyanurate trimer crosspolymer*
PPG-26/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 data that are needed to evaluate the safety of these 12 ingredients are:

- Molecular weight
- If the molecular weight is below 1000 Da, then solubility in formulation, dermal absorption, and/or 28-day dermal toxicity
- If soluble or dermally absorbed, then systemic toxicity, including genotoxicity, carcinogenicity, and reproduction/developmental toxicity, may be needed

Exposure to diisocyanates (such as HDI) in the work place 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 should not be present in the ingredients as manufactured but the Panel stressed that Industry should use good manufacturing practices to ensure that these monomers are not present in the ingredient or in formulation.

HDI/trimethylol hexyllactone crosspolymer is used in 354 formulations, 348 of which are leave-on products and 6 of which are rinse-off products. The highest concentration of use was reported to be 31% for HDI/trimethylol hexyllactone crosspolymer in leave-on products. The next highest reported concentrations of use are for HDI/PPG/polycaprolactone crosspolymer which is used up to 11.8% in face powders and steareth-100/PEG-136/HDI copolymer, which is used up to 2.5% in tonics, dressings and other hair grooming aids.

1-Hydroxyethyl 4,5-Diamino Pyrazole Sulfate

The Panel issued a tentative report for public comment with a 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.

Although carcinogenicity data were not available, the Panel noted that the majority of the results of *in vitro* and *in vivo* genotoxicity tests were negative. Additionally, the available data on acute and repeated dose toxicity, reproductive and developmental toxicity, and irritation and sensitization for 1-hydroxyethyl 4,5-diamino pyrazole sulfate were sufficient to conclude that this ingredient is safe for use in oxidative hair dyes.

The Panel noted that the available epidemiology studies are insufficient to conclude that there is a causal relationship between hair dye use and cancer or other toxicological endpoints, based on lack of strength of the associations and inconsistency of findings.

Polymerized Tetramethylcyclotetrasiloxanes

The Panel issued a tentative report for public comment with the conclusion that the following 3 polymerized tetramethylcyclotetrasiloxanes are safe when used as surface modifiers (encapsulating metal oxides) and that the data are insufficient to determine safety if these ingredients are used independently for other functions as listed in the *International Cosmetic Ingredient Dictionary and Handbook (INCI Dictionary)*; e.g., antifoaming agents, hair conditioning agents, and viscosity increasing agents – nonaqueous).

polysilicone-2
polysilicone-4
polysilicone-5

Negative HRIPT studies and information indicating that when combined, these silicone polymers and the metal oxide particles upon which they are coated, are large and not likely to penetrate the skin, addressed concerns about potential systemic toxicity when these ingredients are used as surface modifiers.

The INCI Dictionary monographs for these ingredients were recently amended to include the function of surface modifier. These amendments will be seen in the next iteration of the INCI Dictionary. The note “[This ingredient] may be used as a coating agent polymerized in situ typically on metal oxides or other materials” has been added to the entries for each ingredient. However, the other recited functions for these ingredients, antifoaming agents, hair conditioning agents, and viscosity increasing agents – nonaqueous, which are inconsistent with large surface coated particles, have not been removed.

The data needed to determine the safe use of these 3 ingredients for functions other than surface modifiers are:

- Chemistry, including average molecular weight and distribution
- Repeated dose inhalation
- Method of manufacture
- Absorption/metabolism. If dermally absorbed: reproductive toxicity, 28-day dermal toxicity, and genotoxicity
- Impurity or all three ingredients

Trimellitic Anhydride Copolymers

The Panel issued a tentative report with a conclusion that the following 6 ingredients are safe in nail products in the present practices of use and concentration described in this safety assessment, but the data are insufficient to determine safety for use in all other types of cosmetic formulations:

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/sebacic acid/trimellitic anhydride copolymer*
trimethylpentanediol/isophthalic acid/trimellitic anhydride 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 safe for use in nail products at concentrations comparable to others in this group.

The data needed to evaluate the safety of these ingredients for uses other than in nail products are:

- Molecular weight;
- Method of manufacture and 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.

Negative irritation and sensitization data on nail product formulations addressed the Panel's concerns about the safe use of these ingredients in nail products. However, the data listed above would be needed to review the safety of these ingredients for use in formulations other than nail products.

Based on data from the FDA VCRP data 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 these ingredients are used in formulations that result in dermal contact. If these ingredients are used in formulations other than nail products, concentration of use data would be necessary.

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 **February 8, 2016, or sooner if possible**. These reports are scheduled for review by the CIR Expert Panel at its **March 31-April 1, 2016** meeting.*

Citrus Flower- and Leaf-Derived Ingredients

The CIR Expert Panel requested additional data to support the safety of the following 32 *Citrus* flower- and leaf-derived ingredients:

citrus aurantifolia (lime) flower extract	citrus grandis (grapefruit) leaf extract
citrus aurantifolia (lime) leaf oil	citrus hystrix leaf extract
citrus aurantium amara (bitter orange) flower extract	citrus junos flower oil
citrus aurantium amara (bitter orange) flower oil	citrus limon (lemon) flower water
citrus aurantium amara (bitter orange) flower water	citrus limon (lemon) leaf extract
citrus aurantium amara (bitter orange) flower wax	citrus limon (lemon) leaf cell extract
citrus aurantium bergamia (bergamot) leaf cell extract	citrus natsudaikai flower water
citrus aurantium bergamia (bergamot) leaf extract	citrus natsudaikai flower oil
citrus aurantium bergamia (bergamot) leaf oil	citrus reticulata (tangerine) leaf oil
citrus aurantium dulcis (orange) flower extract	citrus reticulata (tangerine) leaf water
citrus aurantium dulcis (orange) flower oil	citrus sinensis (orange) flower water
citrus aurantium dulcis (orange) flower wax	citrus tamurana flower extract
citrus aurantium dulcis (orange) flower	citrus unshiu flower extract
citrus aurantium dulcis (orange) leaf extract	citrus unshiu flower powder
citrus clementina leaf cell extract	citrus unshiu flower water
citrus depressa flower water	citrus unshiu leaf extract

The additional data needed are:

- Method of manufacturing
- Chemical composition and impurities
- Irritation and sensitization, especially human repeated insult patch tests (HRIPT) on citrus aurantium amara (bitter orange) flower extract and citrus aurantium amara (bitter orange) flower water at maximum use concentrations or greater

Citrus Peel-Derived Ingredients

The CIR Expert Panel requested additional data to support the safety of the following 47 *Citrus* peel-derived ingredients:

citrus aurantifolia (lime) peel	citrus grandis (grapefruit) peel powder
citrus aurantifolia (lime) peel extract	citrus hassaku/natsudaikai peel powder
citrus aurantifolia (lime) peel powder	citrus iyo peel extract
citrus aurantifolia (lime) peel water	citrus iyo peel water
citrus aurantium amara (bitter orange) peel	citrus jabara peel extract
citrus aurantium amara (bitter orange) peel extract	citrus jabara peel powder
citrus aurantium amara (bitter orange) peel powder	citrus jabara peel water
citrus aurantium bergamia (bergamot) peel water	citrus junos peel extract
citrus aurantium dulcis (orange) peel extract	citrus junos peel powder
citrus aurantium dulcis (orange) peel powder	citrus junos peel water
citrus aurantium dulcis (orange) peel wax	citrus limon (lemon) peel
citrus aurantium sinensis peel extract	citrus limon (lemon) peel extract
citrus aurantium tachibana peel extract	citrus limon (lemon) peel powder
citrus depressa peel extract	citrus limon (lemon) peel water
citrus depressa peel powder	citrus limon (lemon) peel wax
citrus grandis (grapefruit) peel	citrus natsudaikai peel extract
citrus grandis (grapefruit) peel extract	citrus nobilis (mandarin orange) peel extract

citrus nobilis (mandarin orange) peel powder
citrus paradisi (grapefruit) peel extract
citrus reticulata (tangerine) peel extract
citrus reticulata (tangerine) peel powder
citrus shunkokan peel extract
citrus sunki peel extract
citrus tachibana/reticulata peel powder

citrus tangelo peel powder
citrus tangerina (tangerine) peel
citrus tangerina (tangerine) peel extract
citrus unshiu peel extract
citrus unshiu peel powder
citrus unshiu peel water

The additional data needed are:

- Method of manufacturing
- Chemical composition and impurities
- Irritation and sensitization, especially human repeated insult patch tests (HRIPT) on citrus aurantium dulcis (orange) peel extract, citrus grandis (grapefruit) peel extract, citrus limon (lemon) peel extract, and citrus unshiu peel extract at maximum use concentrations or greater

Citrus Plant- and Seed-Derived Ingredients

The Panel requested additional data to support the safety of the following 33 *Citrus* plant- and seed-derived ingredients:

citrus aurantifolia (lime) oil
citrus aurantium (bitter orange) oil
citrus aurantium amara (bitter orange) leaf/twig extract
citrus aurantium amara (bitter orange) leaf/twig oil
citrus aurantium dulcis (orange) flower/leaf/stem powder
citrus aurantium dulcis (orange) oil
citrus aurantium dulcis (orange) seed extract
citrus aurantium sinensis powder
citrus australasica seed oil
citrus depressa seed oil
citrus glauca seed oil
citrus grandis (grapefruit)
citrus grandis (grapefruit) extract
citrus grandis peel/seed extract
citrus grandis (grapefruit) seed extract
citrus iyo oil
citrus jabara pericarp extract

citrus junos extract
citrus junos seed extract
citrus junos seed oil
citrus limon (lemon) flower/leaf/stem extract
citrus limon (lemon) flower/leaf/stem oil
citrus limon (lemon) leaf/peel/stem oil
citrus nobilis (mandarin orange)
citrus nobilis (mandarin orange) oil
citrus nobilis (mandarin orange) water
citrus paradisi (grapefruit) seed extract
citrus sunki seed extract
citrus sunki seed oil
citrus reticulata (tangerine) extract
citrus tangerina (tangerine) extract
citrus unshiu extract
citrus unshiu pericarp extract

The additional data needed are:

- Method of manufacturing
- Chemical composition and impurities
- Irritation and sensitization, especially human repeated insult patch tests (HRIPT) on citrus aurantium amara (bitter orange) leaf/twig oil and citrus grandis (grapefruit) seed extract at maximum use concentrations or greater
- If the composition for these *Citrus* plant- and seed-derived ingredients are significantly different from that of the *Citrus* peel-, flower-, and leaf-derived ingredients, then data on systemic endpoints such as a 28-day dermal toxicity, reproductive and developmental toxicity, and genotoxicity, as well as UV absorption spectra are needed

Helianthus annuus (Sunflower)-Derived Ingredients

The Panel requested additional data to support the safety of the following 13 *Helianthus annuus* (sunflower)-derived ingredients:

helianthus annuus (sunflower) seed extract
helianthus annuus (sunflower) extract
helianthus annuus (sunflower) flower extract
helianthus annuus (sunflower) leaf/stem extract*
helianthus annuus (sunflower) sprout 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
ozonized sunflower seed oil

The additional data needed are:

- HRIPT of hydrogenated sunflower seed extract at least 1%
- Method of manufacture including clarification of the source material (whole plant vs “bark”) of helianthus annuus (sunflower) extract
- Composition of these ingredients, especially protein content (including 2S albumin)
- Impurities

137th Meeting Notes

Director's Report

Dr. Gill highlighted the many accomplishments in 2015. The Panel assessed the safety of over 500 ingredients, reaffirmed the decision on methylisothiazolinone considering the recent SCCS opinion on this ingredient, provided guidance on the CIR ingredient strategies and report format, rendered a decision on the first review of ingredients incorporating a framework for evaluating analogs for read-across assessments, and responded to numerous consumer group concerns. Presentations given in 2015 included infant skin, Quantitative Risk Assessment (QRA), and plant cell cultures. Regarding the status of the 14 ingredients found to be insufficient in 2013 and 2014, additional information submitted to support the safety of 6 *Chamomilla recutita* ingredients will be reviewed in 2016. In accordance with CIR procedures, the 7 *Camellia sinensis*-derived ingredients, and the ingredient avena sativa (oat) meristem cell extract will be categorized as Use Not Supported by Data or No Reported Use at the end of 2016 if additional data are not submitted.

Dr. Gill discussed the 2016 Panel meeting scheduling and the challenge it presents. Because the time between some meetings is less than usual, CIR may change the review cycle for some reports. The 2016 Panel meetings will be held at the Melrose Georgetown Hotel, in Washington, D.C.

Finally, the 2015 Compendium is scheduled to be released before the end of January. This document presents the Abstracts, Discussions and Conclusions of all safety assessments reviewed by the CIR Expert Panel. It also includes a Quick Reference Table that provides the safety conclusions for all ingredients reviewed by the CIR Expert Panel.

Other Items

The Panel reviewed a second draft of the revised CIR report format. Additional changes suggested at this meeting and comments on the draft from the CIR Science and Support Committee (CIR SSC) will be provided to the Panel to review at the March 2016 meeting.

In response to the Panel's request at the September 2015 meeting for information on cosmetic powder exposures, the CIR SSC submitted estimates of the inhalation exposures to respirable particles from the use of loose cosmetic powders. The Panel considered the data and asked CIR to update the CIR Aerosols Precedents document and Framework for guiding the development of CIR safety assessments to address this issue. The Panel plans further discussion on cosmetic powder exposure at the March 2016 meeting.

Scientific Literature Reviews

- **These literature reviews are currently posted on the CIR website at <http://www.cir-safety.org/ingredients/glossary/all>**

Safety Assessment of Keratin and Keratin-Derived Ingredients as Used in Cosmetics Safety Assessment of Phosphoric Acid and Its Simple Salts as Used in Cosmetics

Draft reports for these ingredient families, along with any unpublished data submitted by interested parties, may be presented to the Panel at its meeting on March 31-April 1, 2016.

- **These literature reviews are currently under development and some may be reviewed during the first half of 2016.**

Brown Algae ingredients
Acryloyldimethyltaurate Polymers
Alkoxy Alkyl Silanes
Ginkgo biloba-Derived Ingredients
Polyglyceryl Fatty Acid Esters
Rosa canina-Derived Ingredients
Saccharide Esters
Shea-Derived Ingredients
Simple Carbonate Salts

- **Re-reviews scheduled for the next Panel meeting**

Sodium Sulfate
Sarcosine and Sarcosinate Amides

Next CIR Expert Panel Meeting

Thursday and Friday, March 31- April 1, 2016, at The Melrose Georgetown Hotel, Washington, DC 20037 --- Please contact Carla Jackson (jacksonc@cir-safety.org) before the meeting if you plan to attend.