Announcement

Cosmetic Ingredient Review Expert Panel
133rd Meeting (December 8-9, 2014) - Findings

December 12, 2014

- **Final Safety Assessments**
  - ***Avena sativa* (Oat)-Derived Ingredients – 21 ingredients**
  - **Glycerin – 1 ingredient**
  - **Hydroquinone – 1 ingredient**
  - ***p*-Hydroxyanisole – 1 ingredient**
  - **PCA and Its Salts – 5 ingredients**
  - **PEGylated Alkyl Glycerides – 60 ingredients**
  - **Polyoxyalkylene Siloxane Copolymers, Alkyl-Polyoxyalkylene Siloxane Copolymers, and Related Ingredients – 111 ingredients**
  - **Propylene Glycol Esters – 32 ingredients**
  - **Sorbitan Esters – 20 ingredients**

- **Tentative Safety Assessments**
  - **Ceramides – 23 ingredients**
  - **Lecithin and Other Phosphoglycerides – 17 ingredients**
  - **PEG Diesters – 55 ingredients**
  - **PEGs Cocamine – 47 ingredients**
  - **Sodium Benzotriazolyl Butylphenol Sulfonate – 1 ingredient**

- **Insufficient Data Announcement**
  - ***Centella asiatica*-Derived Ingredients – 9 ingredients**

- **Re-review Summaries – none**

- **133rd Meeting Notes**
  - **Director's report**
  - **Reports Tabled**
    - **Polysaccharide gums – 103 ingredients**
  - **Re-reviews for the next Panel meeting**
  - **Scientific Literature Reviews posted on the CIR website**
  - **Scientific Literature Reviews under development**
  - **Next CIR Expert Panel Meeting – Monday and Tuesday, March 16 - 17, 2015**

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 Unpublished data cited as references in CIR safety assessments are available for review.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

***Avena Sativa*–Derived Ingredients**

The Panel issued a final safety assessment with the conclusion that the following 20 (of 21) *Avena sativa*-derived ingredients are safe in cosmetics in the present practices of use and concentration when formulated to be nonsensitizing:

avena sativa (oat) bran

avena sativa (oat) bran extract

avena sativa (oat) flower/leaf/stem juice*
avena sativa (oat) kernel extract
avena sativa (oat) kernel flour
avena sativa (oat) kernel meal
avena sativa (oat) kernel protein
avena sativa (oat) leaf extract
avena sativa (oat) leaf/stalk extract*
avena sativa (oat) leaf/stem extract*
avena sativa (oat) meal extract
avena sativa (oat) peptide
avena sativa (oat) protein extract
avena sativa (oat) seed extract*
avena sativa (oat) seed water*
avena sativa (oat) sprout oil*
avena sativa (oat) straw extract
hydrolyzed oat protein
hydrolyzed oat flour
hydrolyzed oats

*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 data are insufficient for determining the safety of avena sativa (oat) meristem cell extract. The additional data needed are (1) composition, and (2) concentrations of use.

These ingredients function mostly as abrasives, antioxidants, skin-conditioning agents, absorbents, and bulking agents. Avena sativa (oat) kernel extract has the most reported uses (499) in cosmetic products. The highest reported use concentration was 25% in face and neck products.

A. sativa grains are used extensively in both animal feed and human food and the plant parts are used in animal feed, resulting in much larger oral exposures than would result from cosmetic uses. Therefore, the primary focus of this safety assessment was on evaluating the potential for these ingredients to cause irritation and sensitization.

Glycerin

The Panel issued a final safety assessment with the conclusion that glycerin is safe in cosmetics in the present practices of use and concentration.

Glycerin (also known as glycerol in the literature) had the third largest number of uses (15,654), listed in the FDA VCRP, after water and fragrance. It is reported to be used at concentrations up to 99.4% in skin cleansing products. Glycerin is reported to function as a denaturant, fragrance ingredient, hair conditioning agent, humectant, oral care agent, oral health care drug, skin protectant, skin-conditioning agent – humectant, and viscosity decreasing agent.

Glycerin occurs naturally in all animal and plant matter, largely as glycerides in fats and oils and in intracellular spaces as the backbone of lipids. Glycerin is considered generally recognized as safe (GRAS) by the FDA as a multiple purpose food substance. In addition to dermal protectant and ophthalmic drug products, glycerin is approved for use in anorectal drug products, laxatives and oral health care products.

Hydroquinone

The Panel issued a final amended safety assessment with the conclusion that hydroquinone is safe at concentrations of ≤ 1% in cosmetic formulations designed for discontinuous, brief use followed by rinsing from the skin and hair. Hydroquinone is safe for use in nail adhesives and as a polymerization inhibitor in artificial nail coatings that are cured by LED (light emitting diode) light. Hydroquinone is unsafe for use in other leave-on cosmetic products.

The Panel remained concerned about the potential risk of squamous cell carcinoma in individuals whose hands are exposed to UVA fluorescent light used to cure artificial nail coatings. In addition, the Panel was concerned that UV bulbs in nail lamps that emit UVA light (320-400 nm) can be easily replaced with UVB and UVC bulbs, because exposures to UVB and UVC can cause ocular and/or dermal damage. The Panel concluded that nail lamp devices with LED bulbs are safe for curing artificial nail coatings in both professional and home settings, because exposures to light from LEDs are not associated with skin cancer. They cautioned that if UV-light sources with fluorescent bulbs are used to cure nail coatings, then photo-protective materials for the skin (e.g., gloves, sunscreen) should also be used.

***p*-Hydroxyanisole**

The Panel issued a final amended safety assessment with the conclusion that *p*-hydroxyanisole is safe for use in nail adhesives and as a polymerization inhibitor in artificial nail coatings that are cured by LED (light emitting diode) light. *p*-Hydroxyanisole is unsafe for use in all other cosmetic products because of the potential for dermal depigmentation.

The Panel remained concerned about the potential risk of squamous cell carcinoma in individuals whose hands are exposed to UVA fluorescent light used to cure artificial nail coatings. In addition, the Panel was concerned that UV bulbs in nail lamps that emit UVA light (320-400 nm) can be easily replaced with UVB and UVC bulbs, because exposures to UVB and UVC can cause ocular and/or dermal damage. The Panel concluded that nail lamp devices with LED bulbs are safe for curing artificial nail coatings in both professional and home settings, because exposures to light from LEDs are not associated with skin cancer. They cautioned that if UV-light sources with fluorescent bulbs are used to cure nail coatings, then photo-protective materials for the skin (e.g., gloves, sunscreen) should also be used.

PCA (2-pyrrolidone-5-carboxylic acid) and Its Salts

The Panel issued a final amended safety assessment with the conclusion that the following PCA and its four salts are safe in cosmetics in the present practices of use and concentration, and these ingredients should not be used in cosmetic products in which *N*-nitroso compounds can be formed.

PCA
sodium PCA
calcium PCA
magnesium PCA

potassium PCA

In 1999, the Panel concluded that PCA and sodium PCA were safe as used in cosmetics, and that these ingredients should not be used in cosmetic products in which *N*-nitroso compounds can be formed. The Panel acknowledged the increase in the maximum concentration of use of PCA and sodium PCA from 2.5% in moisturizer formulations in 1999 to 3% sodium PCA in skin cleansing preparations in 2014, and determined that this increase did not present safety concerns. The Panel reaffirmed the 1999 conclusion and determined that the data from that safety assessment and the new data presented in the report support the safety of the three additional salts.

PEGylated Alkyl Glycerides

The Panel issued a final safety assessment with the conclusion that the following 60 PEGylated alkyl glycerides are safe in cosmetics in the present practices of use and concentration when formulated to be non-irritating:

PEG-6 almond glycerides*
PEG-20 almond glycerides
PEG-35 almond glycerides*
PEG-60 almond glycerides
PEG-192 apricot kernel glycerides
PEG-11 avocado glycerides*
PEG-14 avocado glycerides*
PEG-11 babassu glycerides*
PEG-42 babassu glycerides*
PEG-4 caprylic/capric glycerides*
PEG-6 caprylic/capric glycerides
PEG-7 caprylic/capric glycerides
PEG-8 caprylic/capric glycerides
PEG-11 cocoa butter glycerides*
PEG-75 cocoa butter glycerides
PEG-7 cocoglycerides*
PEG-9 cocoglycerides*
PEG-20 corn glycerides*
PEG-60 corn glycerides*
PEG-20 evening primrose glycerides*
PEG-60 evening primrose glycerides*
PEG-3 glyceryl cocoate
PEG-7 glyceryl cocoate
PEG-30 glyceryl cocoate
PEG-40 glyceryl cocoate
PEG-78 glyceryl cocoate*
PEG-80 glyceryl cocoate
PEG-5 hydrogenated corn glycerides*
PEG-8 hydrogenated fish glycerides*
PEG-20 hydrogenated palm glycerides
PEG-6 hydrogenated palm/palm kernel glyceride*
PEG-16 macadamia glycerides
PEG-70 mango glycerides
PEG-13 mink glycerides*
PEG-25 moringa glycerides*
PEG-42 mushroom glycerides*
PEG-2 olive glycerides*
PEG-6 olive glycerides*
PEG-7 olive glycerides*
PEG-10 olive glycerides
PEG-40 olive glycerides*
PEG-18 palm glycerides*
PEG-12 palm kernel glycerides*
PEG-45 palm kernel glycerides
PEG-60 passiflora edulis seed glycerides*
PEG-60 passiflora incarnata seed glycerides*
PEG-45 safflower glycerides*
PEG-60 shea butter glycerides
PEG-75 shea butter glycerides
PEG-75 shorea butter glycerides*
PEG-35 soy glycerides
PEG-75 soy glycerides*
PEG-2 sunflower glycerides*
PEG-7 sunflower glycerides*
PEG-10 sunflower glycerides
PEG-13 sunflower glycerides
PEG-5 tsubakiate glycerides*
PEG-10 tsubakiate glycerides*
PEG-20 tsubakiate glycerides*
PEG-60 tsubakiate glycerides*

*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 safety assessment includes five previously-reviewed PEG glyceryl cocoates, namely PEG-7 glyceryl cocoate, PEG-30 glyceryl cocoate, PEG-40 glyceryl cocoate, PEG-78 glyceryl cocoate, and PEG-80 glyceryl cocoate. The conclusion stated above supersedes the 1999 conclusion for these 5 ingredients. Data included in this safety assessment addressed the Panel's concerns about the sensitization potential of these ingredients at the current concentrations of use.

The Panel reaffirmed that, although carcinogenicity data were not available, these ingredients were not mutagenic and lacked structural alerts for genotoxicity.

Polyoxyalkylene Siloxane Copolymers, Alkyl-Polyoxyalkylene Siloxane Copolymers, and Related Ingredients

The Panel issued a final safety assessment with the conclusion that the following 111 polyoxalkylene siloxane copolymers, alkyl-polyoxyalkylene siloxane copolymers, and related ingredients are safe in cosmetics in the present practices of use and concentration:

behenoxy dimethicone
behenoxy PEG-10 dimethicone*
bis-cetyl/PEG-8 cetyl PEG-8 dimethicone*
bis-hydroxyethoxypropyl dimethicone
bis-isobutyl PEG/PPG-10/7/dimethicone copolymer*
bis-isobutyl PEG-13/dimethicone copolymer*
bis-isobutyl PEG-24/PPG-7/dimethicone copolymer*
bis-PEG-1 dimethicone*
bis-PEG-4 dimethicone
bis-PEG-8 dimethicone*
bis-PEG-10 dimethicone*
bis-PEG-12 dimethicone
bis-PEG-12 dimethicone beeswax
bis-PEG-12 dimethicone candelillate
bis-PEG-15 methyl ether dimethicone
bis-PEG-20 dimethicone*
bis-PEG-8 PEG-8 dimethicone*
bis-PEG/PPG-14/14 dimethicone
bis-PEG/PPG-15/5 dimethicone*
bis-PEG/PPG-16/16 PEG/PPG-16/16 dimethicone
bis-PEG/PPG-18/6 dimethicone*
bis-PEG/PPG-20/20 dimethicone
bis-PEG/PPG-20/5 PEG/PPG-20/5 dimethicone*
bis-stearoxy dimethicone*
bis-stearoxyethyl dimethicone*
cetyl PEG/PPG-10/1 dimethicone
cetyl PEG/PPG-15/15 butyl ether dimethicone*
cetyl PEG/PPG-7/3 dimethicone*
cetyl PEG-8 dimethicone*
lauryl isopentyl-PEG/PPG-18/18 methicone*
lauryl PEG/PPG-18/18 methicone
lauryl PEG-10 methyl ether dimethicone*

lauryl PEG-10 tris(trimethylsiloxy)silylethyl dimethicone*
lauryl PEG-8 dimethicone
lauryl PEG-8 PPG-8 dimethicone*
lauryl PEG-9 polydimethylsiloxyethyl dimethicone
lauryl polyglyceryl-3 polydimethylsiloxyethyl dimethicone*
methoxy PEG-11 methoxy PPG-24 dimethicone*
methoxy PEG/PPG-25/4 dimethicone
methoxy PEG-13 ethyl polysilsesquioxane*
PEG/PPG-10/2 dimethicone*
PEG/PPG-10/3 oleyl ether dimethicone*
PEG/PPG-12/16 dimethicone*
PEG/PPG-12/18 dimethicone*
PEG/PPG-14/4 dimethicone
PEG/PPG-15/15 dimethicone
PEG/PPG-15/5 dimethicone*
PEG/PPG-16/2 dimethicone*
PEG/PPG-16/8 dimethicone*
PEG/PPG-17/18 dimethicone
PEG/PPG-18/12 dimethicone*
PEG/PPG-18/18 dimethicone
PEG/PPG-18/6 dimethicone*
PEG/PPG-19/19 dimethicone
PEG/PPG-20/15 dimethicone
PEG/PPG-20/20 dimethicone
PEG/PPG-20/22 butyl ether dimethicone*
PEG/PPG-20/22 methyl ether dimethicone*
PEG/PPG-20/23 dimethicone
PEG/PPG-20/29 dimethicone*
PEG/PPG-20/6 dimethicone
PEG/PPG-22/22 butyl ether dimethicone*
PEG/PPG-22/23 dimethicone
PEG/PPG-22/24 dimethicone
PEG/PPG-23/23 butyl ether dimethicone*
PEG/PPG-23/6 dimethicone*
PEG/PPG-24/18 butyl ether dimethicone*
PEG/PPG-25/25 dimethicone
PEG/PPG-27/27 dimethicone*
PEG/PPG-27/9 butyl ether dimethicone*
PEG/PPG-3/10 dimethicone*
PEG/PPG-30/10 dimethicone
PEG/PPG-4/12 dimethicone
PEG/PPG-6/4 dimethicone*
PEG/PPG-6/11 dimethicone*
PEG/PPG-8/14 dimethicone
PEG/PPG-8/26 dimethicone*
PEG-10 dimethicone
PEG-10 methyl ether dimethicone
PEG-10 polydimethylsiloxyethyl dimethicone/bis-vinyl dimethicone crosspolymer*
PEG-11 methyl ether dimethicone
PEG-12 dimethicone
PEG-14 dimethicone
PEG-17 dimethicone
PEG-3 dimethicone
PEG-32 methyl ether dimethicone
PEG-4 PEG-12 dimethicone*
PEG-6 dimethicone*
PEG-6 methyl ether dimethicone
PEG-7 dimethicone
PEG-7 methyl ether dimethicone*
PEG-8 cetyl dimethicone
PEG-8 dimethicone
PEG-8 dimethicone dimer dilinoleate*
PEG-8 dimethicone/dimer dilinoleic acid copolymer
PEG-8 methicone
PEG-8 methyl ether dimethicone*
PEG-8 PEG-4 dimethicone*
PEG-8 PPG-8 dimethicone*
PEG-9 dimethicone
PEG-9 methyl ether dimethicone*
PPG-25 dimethicone*
PPG-27 dimethicone*
PPG-4 oleth-10 dimethicone*
PEG-9 polydimethylsiloxyethyl dimethicone
polysilicone-13
PPG-12 butyl ether dimethicone*
PPG-12 dimethicone
PPG-2 dimethicone
stearoxy dimethicone
stearoxymethicone/dimethicone 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.

These ingredients function as hair conditioning agents, viscosity increasing agents, emulsion stabilizers, and film formers. The highest frequencies of use were reported in lipsticks and products used around the eyes. The highest maximum concentrations of use were reported for stearoxy dimethicone (22% in hair conditioners), cetyl PEG/PPG 10/1 dimethicone (15% in eyebrow pencils and 13.6% in eye shadow), PEG/PPG-17/18 dimethicone (14% in perfumes and 13% in hair products), and bis-hydroxyethyoxypropyl dimethicone (12% in blushers).

The Panel discussed their initial concern about the presence of up to 30% residual allyl alcohol ethoxylates as impurities. The manufacturing process of these copolymers involves the silylation of preformed polyethers with dimethicone, which yields products containing up to 30% of the polyether starting material. . The results of toxicity studies on these ingredients, which are known to contain large concentrations of the residual material, assured the Panel that residual polyethers are not a concern.

Propylene Glycol Esters

The CIR Expert Panel issued a final amended safety assessment for the following 32 propylene glycol esters with the conclusion that these ingredients are safe as used in cosmetics when formulated to be non-irritating:

almond oil propylene glycol esters*
apricot kernel oil propylene glycol esters*
avocado oil propylene glycol esters*
olive oil propylene glycol esters*
propylene glycol behenate*
propylene glycol caprylate*
propylene glycol cocoate*
propylene glycol dicaprate
propylene glycol dicaproate
propylene glycol dicaprylate
propylene glycol dicaprylate/dicaprate
propylene glycol dicocoate*
propylene glycol diethylhexanoate
propylene glycol diisononanoate*
propylene glycol diisostearate*
propylene glycol dilaurate*
propylene glycol dioleate
propylene glycol dipelargonate
propylene glycol distearate*
propylene glycol diundecanoate*
propylene glycol heptanoate*
propylene glycol linoleate*
propylene glycol linolenate*
propylene glycol isostearate
propylene glycol laurate
propylene glycol myristate
propylene glycol oleate
propylene glycol oleate SE (self-emulsifying)*
propylene glycol soyate*
propylene glycol stearate
propylene glycol stearate SE
soybean oil propylene glycol 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 frequency of use of propylene glycol dicaprylate/dicaprate increased from 202 in 1995 to 525 in 2014. The use frequency of propylene glycol dicaprylate increased from 1 in 1995 to 102 in 2014. The use frequencies of the other previously-reviewed ingredients in this safety assessment have decreased. These propylene glycol esters mostly function as skin-conditioning agents (emollient) and as surfactants (emulsifying agent).

The Panel acknowledged that the original safety assessment relied upon safety data available for ingredients representing chemical sub-structure moieties of these ingredients (e.g., propylene glycol and the acids of the esters). The Panel agreed that this approach is acceptable for the PG esters in this safety assessment, coupled with the original data on propylene glycol stearate. In addition, the new repeated-dose, reproductive-toxicity, and irritation data for propylene glycol dicaprylate/dicaprate did not raise concerns about the safety of ingredients in this group.

The Panel recognized that PG esters can enhance the dermal penetration of other ingredients, and cautioned that care should be taken when formulating cosmetic products that may contain the PG esters ingredients with other ingredients for which dermal absorption was a concern.

Sorbitan Esters

The Panel issued a final amended safety assessment with the conclusion that the following 20 sorbitan esters are safe in cosmetics in the present practices of use and concentration:

sorbitan caprylate
sorbitan cocoate*
sorbitan diisostearate*
sorbitan dioleate*
sorbitan distearate*
sorbitan isostearate
sorbitan laurate
sorbitan oleate
sorbitan olivate
sorbitan palmate
sorbitan palmitate
sorbitan sesquicaprylate*
sorbitan sesquiisostearate
sorbitan sesquioleate
sorbitan sesquistearate*
sorbitan stearate
sorbitan triisostearate
sorbitan trioleate
sorbitan tristearate
sorbitan 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.

In 1985, the Panel determined that seven sorbitan esters were safe as used in cosmetics. In 2002, the Panel reviewed the safety of 10 additional sorbitan esters and issued an addendum to the 1985 report, concluding that the sorbitan fatty acid esters were safe as used in cosmetic ingredients. The Panel reaffirmed the safe as used conclusions of the 1985 and 2002 safety assessments and determined that the data from those safety assessments, together with the new data presented on the sorbitan esters, support the safety of sorbitan palmate, sorbitan sesquicaprylate, and sorbitan undecylenate.

The Panel decided to not include sorbitan theobroma grandiflorum seedate in this amended safety assessment, because it may have skin-bleaching action, which is not considered to be a cosmetic function in the U.S.

Tentative Safety Assessments

*Tentative safety assessments will be posted on the CIR website at www.cir-safety.org on or before **December 19, 2014**. 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 **January 30, 2015, or sooner if possible.** These reports may be scheduled for review by the CIR Expert Panel at its **March 16-17, 2015** meeting.*

Ceramides

The Panel issued a tentative safety assessment for public comment with the conclusion that the following 23 ceramides are safe in cosmetics in the present practices of use and concentration:

ceramide 1
ceramide 2
ceramide 3
ceramide 4*
ceramide 5*
ceramide 1A
ceramide 6 II
ceramide AP
ceramide EOP
ceramide EOS
ceramide NP
ceramide NG*
ceramide NS
ceramide AS*
ceramide NS dilaurate*
caprooyl phytosphingosine
caprooyl sphingosine
hydroxypalmitoyl sphinganine
2-oleamido-1,3-octadecanediol
caproyl sphingosine*
hydroxylauroyl phytosphingosine*
hydroxycapryloyl phytosphingosine*
hydroxycaproyl phytosphingosine*

*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 there was a screening reproductive and developmental toxicity study on 2-Oleamido-1,3-Octadecanediol, however there was no data on carcinogenicity. The Panel considered the negative results of a reproductive and developmental toxicity study in rats and of in vitro genotoxicity assays,

as well as the findings of no systemic toxicity at high doses in single and repeated oral dose animal studies, little to no irritation in ocular and dermal animal studies, no dermal irritation in human studies, and no dermal sensitization in multiple animal studies to support their conclusion for these ingredients.

The Panel noted that the names of ceramide ingredients have changed recently. For example, the INCI name, Ceramide 1 has been retired and replaced by the name Ceramide EOP. For an interim period, products on the market may be labelled with either name, Ceramide 1 or Ceramide EOP, although both names refer to the same ingredient.

The Panel determined that these ceramide ingredients are safe as used, assuming that the ingredients are not derived from bovine central nervous system tissues.

Lecithin and Other Phosphoglycerides

The Panel issued a tentative safety assessment for public comment with the conclusion that the following 17 ingredients are safe in the present practices of use and concentration:

Lecithin
Hydrogenated Lecithin
Lysolecithin
Hydrogenated Lysolecithin
Phospholipids
Hydrolyzed Phospholipids
Phosphatidic Acid
Lysophosphatidic Acid
Phosphatidylglycerol
Lysophosphatidylglycerol
Phosphatidylserine
Ammonium Phosphatidyl Rapeseedate
Phosphatidylcholine
Hydrogenated Phosphatidylcholine
Hydrogenated Lysophosphatidylcholine
Lysophosphatidylethanolamine
Phosphatidylinositol

These ingredients are glycerides of fatty acids that are linked to phosphoric acid or to a phosphoric ester. Lecithin, for example, is a complex mixture of phosphatides consisting chiefly of phosphatidylcholine, phosphatidylethanolamine, phosphatidylserine, and phosphatidylinositol, with various amounts of triglycerides, fatty acids and carbohydrates. These phosphoglycerides function mainly as skin and hair conditioning agents, emulsifying agents, and surfactants in cosmetic products.

In 2001, the Panel published a final report with the conclusion that lecithin and hydrogenated lecithin are safe as used in rinse-off products and safe for use in leave-on products at concentrations ≤ 15%, and the data are insufficient to determine the safety of use in cosmetic products where lecithin and hydrogenated lecithin are likely to be inhaled; lecithin and hydrogenated lecithin should not be used in cosmetic products in which *N*-nitroso compounds may be formed. The data available for lecithin was relevant for assessing the safety of the entire group because of the similarity of its chemical structure to those of the other ingredients in the group. The conclusion stated above supersedes the 2001 conclusion for lecithin and hydrogenated lecithin.

The Panel was concerned that lecithin may be derived from animal tissues from which infectious agents may be transmitted. Industry assured the Panel that the phosphoglycerides used as ingredients in cosmetic products are either egg- or plant-derived. Additionally, the Panel requested clarification of the reported use of lecithin at concentrations up to 50% in leave-on cosmetic products.

PEG Diesters

The Panel issued a tentative amended report for public comment with the conclusion that 55 PEG diesters are safe in cosmetics in the present practices of use and concentration. The ingredients in this report are:

PEG-150 dibehenate*
PEG-3 dicaprylate/caprate*
PEG-4 dicocoate*
PEG-8 dicocoate
PEG-4 diheptanoate
PEG-2 diisononanoate
PEG-2 diisostearate*
PEG-3 diisostearate*
PEG-4 diisostearate*
PEG-6 diisostearate
PEG-8 diisostearate
PEG-12 diisostearate
PEG-90 diisostearate
PEG-175 diisostearate
PEG-2 dilaurate*
PEG-4 dilaurate
PEG-6 dilaurate*
PEG-8 dilaurate
PEG-12 dilaurate*
PEG-16 dilaurate*
PEG-20 dilaurate*
PEG-32 dilaurate*
PEG-75 dilaurate*
PEG-150 dilaurate*
PEG-2 dioleate*
PEG-3 dioleate*
PEG-4 dioleate*
PEG-6 dioleate*
PEG-8 dioleate
PEG-10 dioleate*
PEG-12 dioleate
PEG-20 dioleate*
PEG-32 dioleate*
PEG-75 dioleate*
PEG-150 dioleate*
PEG-3 dipalmitate*
PEG-2 distearate
PEG-3 distearate
PEG-4 distearate
PEG-6 distearate
PEG-8 distearate
PEG-9 distearate*
PEG-12 distearate
PEG-20 distearate*
PEG-32 distearate*
PEG-40 distearate*
PEG-50 distearate
PEG-75 distearate*
PEG-120 distearate
PEG-150 distearate
PEG-175 distearate
PEG-190 distearate*
PEG-250 distearate
PEG-8 ditallate*
PEG-12 ditallate*

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

In this safety assessment, PEG-150 distearate was reported to have the greatest number of uses at 654 (an increase from 187 in 1996). Most of these uses are in bath and personal cleansing products and shampoos. PEG-150 distearate was reported to have the greatest concentration of use at up to 33.2% (an increase from 5% in 1995); the highest concentration of use was in skin cleansing products. PEG-4 dilaurate and PEG-8 dilaurate were each reported to be used at concentrations up to 25% in 1984, and are currently used at concentrations up to 12% and 15%, respectively.

Unlike PEG-8 dioleate and PEG-8 dilaurate, 5% PEG-12 dioleate enhanced the dermal penetration of ketoprofen in a study using nude mice. The Panel noted that formulators should be aware of the potential for enhancing the dermal penetration of other ingredients in cosmetic formulations that contain the ingredients evaluated in this safety assessment.

PEGs Cocamine and Related Ingredients

The Panel issued a tentative amended safety assessment with the conclusion that the following 32 PEGs cocamine and related ingredients are safe in cosmetics in the present practices of use and concentration when formulated to be non-irritating:

PEG-8 cocamine*
PEG-10 cocamine*
PEG-12 cocamine*
PEG-15 cocamine
PEG-20 cocamine*
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-6 oleamine*
PEG-10 oleamine*
PEG-15 oleamine*
PEG-20 oleamine*
PEG-25 oleamine*
PEG-30 oleamine*
PEG-12 palmitamine*
PEG-8 soyamine*
PEG-10 soyamine*
PEG-15 soyamine*
PEG-10 stearamine*
PEG-15 stearamine*
PEG-50 stearamine*
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.

The Panel agreed that gaps in genotoxicity and systemic toxicity data can be filled for these 32 ingredients by applying the SAR-based framework presented to identify and evaluate analogs for read across analyses.

However, the Expert Panel requested additional data to support the safety of the smaller PEGs cocamine and related ingredients, including those listed below.

PEG-2 cocamine
PEG-3 cocamine
PEG-4 cocamine
PEG-5 cocamine
PEG-2 hydrogenated tallow amine
PEG-5 hydrogenated tallow amine
PEG-2 lauramine
PEG-2 oleamine
PEG-5 oleamine
PEG-2 rapseedamine
PEG-2 soyamine
PEG-5 soyamine
PEG-2 stearamine
PEG-5 stearamine
PEG-2 tallow amine

The additional data needed for these ingredients are (1) physical and chemical properties, including impurities (especially nitrosamines), (2) genotoxicity in a mammalian test system (if the results are positive then a dermal carcinogenesis study may be needed), (3) 28-day dermal toxicity using PEG-2 cocamine, and (4) dermal sensitization data on PEG-2 cocamine. The Panel also noted the absence of use concentration data for PEG-2 rapeseedamine, in particular, because this ingredient had the greatest use frequency (255) reported to the VCRP.

The Panel expressed support for developing the SAR-based framework as a systematic approach to identifying possible analogues for read-across assessments, and categorizing the analogues as suitable, suitable with interpretation, and suitable with precondition. However, the Panel emphasized the importance of developing quantitative measures for the key decision-making steps of the approach, characterizing the boundary conditions and assumptions of the models applied, and using actual test data for the class of chemicals to which the ingredients belong to validate computational predictions.

Sodium Benzotriazolyl Butylphenol Sulfonate

The Panel issued a tentative report for public comment with the conclusion that sodium benzotriazolyl butylphenol sulfonate is safe as used in cosmetics.

The Panel expressed concern about studies that indicated the potential for ocular irritation. However, the Panel noted that the concentrations used in these studies that resulted in ocular damage were much greater than the concentrations reported to be used in cosmetics. Additionally, there are no reported uses in products specified for use around the eyes.

Sodium benzotriazolyl butylphenol sulfonate was reported to be used in 67 leave-on products, 377 rinse-off products, and 29 products for the bath and the maximum concentration of use reported was 0.64% in leave-on products, specifically in skin fresheners. It is used in rinse-off products at concentrations up to 0.1%, with the maximum concentration reported for skin cleansing products.

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 ***January 30, 2015, or sooner if possible****. This report is scheduled for review by the CIR Expert Panel at its* ***March 16-17, 2015*** *meeting.*

***Centella asiatica*-derived Ingredients**

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

centella asiatica extract
centella asiatica callus culture
centella asiatica flower/leaf/stem extract
centella asiatica leaf cell culture extract
centella asiatica leaf extract
centella asiatica leaf water
centella asiatica meristem cell culture
centella asiatica meristem cell culture extract
centella asiatica root extract

The data requested are as follows:

- Method of manufacture and impurities of all ingredients, except centella asiatica extract and centella asiatica leaf extract
- Use concentrations of centella asiatica leaf extract
- Ocular irritation tests of centella asiatica extract at the highest maximum use concentration (0.3%) reported for products applied to the eye area
- Systemic toxicity tests for all ingredients, except centella asiatica extract and centella asiatica leaf extract

The Panel is also seeking confirmation that Centella Asiatica Extract is an extract of the whole plant. If this is confirmed, then the toxicity data available for Centella Asiatica Extract may be used to support the safety of other *Centella asiatica*-derived ingredients. The Panel agreed that data from a dermal carcinogenicity study on asiaticoside (saponin component of *Centella asiatica*) using hairless mice should be included in this report; the study is summarized in the 2012 *European Medicines Agency Assessment Report on Centella asiatica (L.) Urban, herba*.

Re-review Summaries - none

133rd Meeting Notes

Director's Report

Dr. Gill welcomed Dr. Nakissa Sadrieh, Director of the Cosmetics Staff in the Office of Cosmetics and Colors, CFSAN, FDA. Dr. Sudrieh attended for Dr. Linda Katz, the FDA Liaison to the CIR Expert Panel.

Dr. Gill discussed the many accomplishments of the Expert Panel in 2014. The Panel rendered safety decisions on a projected 400+ ingredients this year. In 2013 and 2014, 13 ingredients were determined to have insufficient data to support safety conclusions, including 6 *Chamomilla recutita* ingredients and 7 *Camellia sinensis*-derived ingredients, and avena sativa (oat) meristem cell extract. In accordance with CIR procedures, the *Chamomilla recutita* ingredients will be categorized as Use Not Supported by Data or No Reported Use at the end of 2015 if additional data are not submitted. The Panel evaluated presentations on hydrolyzed wheat protein and hydrolyzed wheat gluten as used in cosmetics, the barrier properties of infant skin, and algae. The Panel also reviewed boilerplate and guidance documents on proposed strategies to grouping ingredients in original safety assessments and re-reviews.

Dr. Gill also mentioned that the CIR 2014 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.

Dr. Gill announced that the first meeting in 2015 will be held on March 16 and 17 at the Mayflower Renaissance Hotel. The agenda will include a presentation by Anne Marie Api, Vice President of Human Health Sciences, RIFM. The schedule for the 2015 CIR Expert Panel meetings was distributed at the meeting and is available on the CIR website

Reports tabled

Polysaccharide Gums

The Panel tabled the draft tentative safety assessment on polysaccharide gums pending reorganization of the report and to allow sufficient time for industry to provide additional data.

The Panel noted that dividing these ingredients into 5 proposed categories based on their chemical structures helped to clarify the structural similarities among the ingredients, but the presentation of the safety data in the report was not conducive to evaluating these ingredients based on their structural

similarities. Thus, the ingredients and the safety data will be reorganized under two major headings, namely Modified and Unmodified polysaccharide gums. The ingredients in the Modified subgroup will be further subdivided into Linear, Branched, Cyclic, and Unknown Structural Configuration. The ingredients in the Unmodified sugroup will be subdivided into Linear Polysaccharides and Salts Thereof, Branched - Natural/Unmodified, Cyclic, and Unknown Structural Configuration.

The following ingredients are included in this report:

Linear Polysaccharides and Salts Thereof

Agar
Agarose
Algin
Alginic Acid
Ammonium Alginate
Amylose
Calcium Alginate
Calcium Carrageenan
Carrageenan
Inulin
Magnesium Alginate
Mannan
Polianthes Tuberosa Polysaccharide
Potassium Alginate
Potassium Carrageenan
Sodium Carrageenan
TEA-Alginate

Linear – Modified

Amylodextrin
Hydrolyzed Carrageenan
Hydrolyzed Furcellaran
Maltodextrin
Potassium Undecylenoyl Carrageenan
Sodium Algin Sulfate
Sodium/TEA-Undecylenoyl Carrageenan

Branched Natural/Unmodified

Amylopectin
Aphanothece Sacrum Polysaccharide
Arabinoxylan
Avena Sativa (Oat) Starch
Cichorium Intybus (Chicory) Root Oligosaccharides
Galactoarabinan
Ghatti Gum
Glucomannan
Pectin
Phaseolus Angularis Seed Starch
Phaseolus Radiatus Seed Starch
Pisum Sativum (Pea) Starch
Pueraria Lobata Starch
Solanum Tuberosum (Potato) Starch
Starch Acetate
Sterculia Urens Gum
Tamarindus Indica Seed Gum
Tapioca Starch

Branched – Modified

Calcium Starch Isododecenylsuccinate
Calcium Starch Octenylsuccinate
Corn Starch Modified
Dextrin
Dextrin Behenate
Dextrin Isostearate
Dextrin Laurate
Dextrin Myristate
Dextrin Palmitate
Dextrin Palmitate/Ethylhexanoate
Dextrin Stearate
Glyceryl Dimaltodextrin
Glyceryl Starch
Hydrolyzed Pectin
Hydroxypropyltrimonium Hydrolyzed Corn Starch
TEA-Dextrin Octenylsuccinate
Hydroxypropyltrimonium Hydrolyzed Wheat Starch
Hydroxypropyl Oxidized Starch
Hydroxypropyl Starch
Hydroxypropyltrimonium Maltodextrin Crosspolymer
Laurdimonium Hydroxypropyl Hydrolyzed Wheat Starch
Palmitoyl Inulin
Potassium Dextrin Octenylsuccinate
Potassium Undecylenoyl Alginate
Potato Starch Modified
Propylene Glycol Alginate
Sodium Carboxymethyl Inulin
Sodium Carboxymethyl Starch
Sodium Dextrin Octenylsuccinate
Undecylenoyl Inulin
Sodium Hydrolyzed Potato Starch Dodecenylsuccinate
Sodium Hydroxypropyl Oxidized Starch Succinate
Sodium Oxidized Starch Acetate/Succinate
Sodium Starch Octenylsuccinate
Sodium/TEA-Undecylenoyl Alginate
Starch Acetate/Adipate
Starch Diethylaminoethyl Ether
Starch Hydroxypropyltrimonium Chloride
Starch Laurate
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
Echinacin
Prunus Persica (Peach) Gum

Unknown Structural Configuration – Modified

Hydrogenated Potato Starch
Hydrogenated Starch Hydrolysate
Hydrolyzed Corn Starch Hydroxyethyl Ether
Hydrolyzed Corn Starch Octenylsuccinate
Hydrolyzed Soy Starch
Hydrolyzed Starch
Hydrolyzed Triticum Spelta Starch
Hydrolyzed Wheat Starch

The Panel also requested information on the method of manufacture and impurities of hydrolyzed carrageenan and glucomannan. Further information is sought to better understand the difference between the cosmetic ingredient hydrolyzed carrageenan and degraded carrageenan (poligeenan), because the data provided suggest the induction of colon tumors in a study in which rats received degraded carrageenan (poligeenan) in the diet or in drinking water. However, the Panel noted that the available studies indicate that carrageenan did not cause dose-related gross or microscopic changes in monkeys in a 7.5-year feeding study, suggesting that carrageenan did not degrade to yield a toxic substance in the gut.

The Panel requested additional data to clarify a report that inhalation of konjac flour induced respiratory sensitization in test animals. Glucomannan is the principle component of konjac flour, but it is not clear to what extent the pulmonary hypersensitivity observed in these animals can be attributed to glucomannan, rather than to some other component of the flour.

The Panel invites additional information on the alkylating and other agents, such as epoxides, anhydrides, and chlorinated compounds that are used to modify polysaccharide gums.

Scientific Literature Reviews

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

  Polyene
  Polymerized Tetramethylcyclotetrasiloxane
  Pyrus malus (Apple)-Derived Ingredients

  Draft reports for these ingredient families, along with any unpublished data submitted by interested parties, may be presented to the Panel at its meeting on March 16-17, 2015.

- **These literature reviews are currently under development**

  Alkonium Clays
  Gingko biloba-derived ingredients
  Inorganic Hydroxides
  Polyglyceryl Fatty Acid Esters
  Silk Proteins
  Trialkyl Trimellitates

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

  Bisabolol
  Hydroxystearic Acid
  Isostearamidopropyl Morpholine Lactate
  Nonoxynols
  Polysorbates

Next CIR Expert Panel Meeting

Monday and Tuesday, March 16-17, 2015, at the Mayflower Renaissance Hotel, 1127 Connecticut Avenue, NW, Washington, DC 20036 --- Please contact Carla Jackson (jacksonc@cir-safety.org) at CIR before the meeting if you plan to attend.