MARCH TO JUNE SUPPLEMENT

Introduction
Priorities
Adenosine ingredients
Ascorbyl Glucoside
Basic Brown 17
Caprylhydroxamic Acid
Carica papaya (Papaya)-derived ingredients
Glycerin Ethoxylates
Honey-derived ingredients
Methicones
Methylisothiazolinone
Palm tree (juçara & acai)-derived ingredients
Carica papaya (Papaya)-derived ingredients
Punica granatum (Pomegranate) ingredients
Quaternium-18
Scutellaria baicalensis-derived ingredients
Glycine soya (Soy) – derived ingredients
Sulfites
Tris(Tetramethylhydroxypiperidinol) Citrate
Vanilla-derived ingredients
Wheat ingredients

CIR EXPERT PANEL MEETING
JUNE 8-9, 2020

154th Meeting of the Expert Panel for Cosmetic Ingredient Safety
June 8 - 9, 2020
Virtual via Microsoft Teams
March-to-June Supplement

WELCOME TO THE 154th EXPERT PANEL MEETING

Welcome to the first Expert Panel meeting of 2020! ***Please note the location is new – it is a virtual meeting via the Microsoft Teams meeting platform***. If you are not a member or liaison of the Expert Panel, and plan to attend this virtual meeting, please register in advance at the following link:

https://forms.office.com/Pages/ResponsePage.aspx?id=ByKur1mpMUKMYzC-b_6TPhdjA_BjNLlKq6vrVcM23eVUMEVGRzhRVUpKTUtPS1hTWU43R0U2M1lSTS4u

or via the following QR code:

Please check your email in the coming weeks for ***3*** meeting invitations: 1) Day 1 announcements and Marks team breakout (**the meeting commences herein**), 2) Belsito team breakout, and 3) Day 2 full Panel.

Here is a *sample* meeting invite email message to expect:

Join Microsoft Teams Meeting - Expert Panel - Day 1 - Announcements and Marks Team Breakout

Local numbers | Reset PIN | Learn more about Teams | Meeting options

Cosmetic Ingredient Review

Cosmetic Ingredient Review
1620 L Street, NW, Suite 1200
Washington, DC 20036-4702

The meeting materials for the 154th Expert Panel Meeting to be held on (Monday & Tuesday) June 8 - 9, 2020 were originally posted to the CIR website on February 21st. However, as you may be aware, the March meeting was cancelled due to issues related to the COVID-19 pandemic. The planned content from that cancelled meeting has been carried forward, in-full, to this meeting. Thus, if you have copies of those original documents and would like to use those for the upcoming June meeting, please feel free to do so (as the newly posted reports are substantively unchanged, including pagination). **However, please look to the meeting website (https://www.cir-safety.org/meeting/154th-expert-panel-meeting) to access the Wave 2 document, that was posted prior to the March meeting, and a completely new document, the March-to-June Supplement (herein, below).** Alternatively, if you would prefer to start afresh with the report documents on the current meeting page, that is also possible (as the only changes therein compared to the pre-March documents are the dates and name of the Panel).

On the following pages, please find information received by CIR after cancellation of the March meeting.

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Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Dr. Bart Heldreth, Executive Director, CIR
Date: May 15, 2020
Subject: Draft 2021 Priorities

Comments on the Draft 2021 Priorities were received from the Personal Care Products Council on April 27, 2020 (*priorities062020sup_pcpc*). Although these comments are included for your review, please note that changes have not been made to the document, which had been prepared for the March meeting. Instead, they will be addressed following the June meeting.

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Personal Care Products Council
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TO: Bart Heldreth Ph.D.
Executive Director – Cosmetic Ingredient Review

FROM: CIR Science and Support Committee

DATE: April 27, 2020

SIBJECT: Comments Draft 2021 CIR Priorities

The CIR Science and Support Committee (CIR SSC) appreciates the opportunity to comment on the Draft 2021 Priorities. After reviewing the draft 2021 CIR priorities list, we believe that it is not necessary to review three of the proposed ingredients, Butyl Methoxydibenzoylmethane, Magnesium Chloride and Calcium Sulfate. We also have one suggested addition to the 2021 priority list, Leuconostoc/Radish Root Ferment Filtrate.

B**utyl Methoxydibenzyolmethane:** Although Butyl Methoxydibenzoylmethane has light stabilizer listed as a function, its primary use is as a sunscreen active ingredient with OTC drug status in the United States.[1] Butyl Methoxydibenzoylmethane, under its drug name Avobenzone, is currently the subject of much FDA and industry activity due to recent efforts prompted by the Sunscreen Innovation Act as well as the recent OTC Monograph Reform. As a result of these regulatory activities, new data are expected to be available. Therefore, we strongly recommend that Butyl Methoxydibenzoylmethane not be reviewed by CIR until these efforts are completed. This is consistent with CIR procedures that state that the CIR Expert Panel can exclude from evaluation a cosmetic ingredient which is also listed as an active ingredient in an OTC drug monograph.

Magnesium Chloride and Calcium Sulfate: The review of these two simple salts is not necessary. CIR could better spend its resources and those of the CIR Expert Panel reviewing ingredients that are not normal constituents of the human body.

Leuconostoc/Radish Root Ferment Filtrate: We recommend adding this ingredient to the 2021 priority list. Leuconostoc/Radish Root Ferment Filtrate has 322 uses reported to the VCRP, in the range of the number of uses reported for other ingredients on the proposed 2021 priority list. Antifungal and antimicrobial agents are among the functions listed for this ingredient which may find use as an alternative preservative, and is the reason we are recommending its review.

[1] Please note that frequency of use (FOU) values in the FDA Voluntary Cosmetic Registration Program (VCRP) do not reflect function. The VCRP associates the name Butyl Methoxydibenzoylmethane with the CAS number 70356-09-1, while the name Avobenzone is associated with a surrogate number (VCRP code# 999001-76-0). Therefore, the much larger FOU for Butyl Methoxydibenzyolmethane (5128) in the VCRP compared to Avobenzone (49) may simply be because companies are finding ingredients in the VCRP by CAS number which is associated with the cosmetic ingredient name rather than the drug name.

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Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Priya Cherian, Scientific Writer/Analyst, CIR
Date: May 15, 2020
Subject: Supplement - Safety Assessment of Adenosine Ingredients as Used in Cosmetics

Comments on the Draft Tentative Report of the Safety Assessment of Adenosine Ingredients as Used in Cosmetics were received from the Personal Care Products Council on March 10, 2020 (*adenos062020sup_pcpc*). Although these comments are included for your review, please note that changes have not been made to the existing report, which had been prepared for the March meeting. Instead, they will be addressed following the June meeting.

Personal Care Products Council
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Memorandum

TO: Bart Heldreth, Ph.D.
Executive Director - Cosmetic Ingredient Review

FROM: Alexandra Kowcz, MS, MBA
Industry Liaison to the CIR Expert Panel

DATE: March 10, 2020

SUBJECT: Draft Tentative Report: Safety Assessment of Adenosine Ingredients as Used in Cosmetics (draft prepared for the March 16-17, 2020 CIR Expert Panel meeting)

The Personal Care Products Council respectfully submits the following comments on the draft tentative report, Safety Assessment of Adenosine Ingredients as Used in Cosmetics.

Key Issue

If the Discussion is going to base safety in cosmetics on dietary levels of Adenosine ingredients, the Non-Cosmetic Use section should mention dietary and dietary supplement use of these ingredients.

Perhaps the addition of a 12 week oral study of Adenosine Triphosphate in humans would also help support the safety of this ingredient (complete study at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3849389/pdf/1743-7075-10-57.pdf). Although the focus of this study was muscle function, they also included clinical chemistry and hematology to assess safety.

Wilson JM, Joy JM, Lowery RP. 2013. Effects of oral adenosine-5'-triphosphate supplementation on athletic performance, skeletal muscle hypertrophy and recovery in resistance-trained men. *Nutrition & Metabolism* 10:57.

Additional Considerations

Introduction - Please correct: “structurally similarities”

Cytotoxicity; Summary - Please add the word “growth” to “Cell inhibition” in both the Cytotoxicity and Summary sections.

Discussion - Perhaps the clinical inhalation exposure should be mentioned in the Discussion section.

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Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Wilbur Johnson, Jr.
Senior Scientific Analyst, CIR
Date: May 15, 2020
Subject: Supplement - Safety Assessment of Ascorbyl Glucoside and Sodium Ascorbyl Glucoside as Used in Cosmetics

Comments on the Draft Report of the Safety Assessment of Ascorbyl Glucoside and Sodium Ascorbyl Glucoside as Used in Cosmetics were received from the Personal Care Products Council on March 10, 2020 (*ascorb062020sup_pcpc*). Although these comments are included for your review, please note that changes have not been made to the existing report, which had been prepared for the March meeting. Instead, they will be addressed following the June meeting.

Personal Care Products Council
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Memorandum

TO: Bart Heldreth, Ph.D.
Executive Director - Cosmetic Ingredient Review

FROM: Alexandra Kowcz, MS, MBA
Industry Liaison to the CIR Expert Panel

DATE: March 10, 2020

SUBJECT: Draft Report: Safety Assessment of Ascorbyl Glucoside and Sodium Ascorbyl Glucoside as Used in Cosmetics (draft prepared for the March 16-17, 2020 CIR Expert Panel meeting)

The Personal Care Products Council respectfully submits the following comments on the draft report, Safety Assessment of Ascorbyl Glucoside and Sodium Ascorbyl Glucoside as Used in Cosmetics.

Key Issue

As studies in this report clearly show that Ascorbyl Glucoside is metabolized to ascorbic acid in the skin and in the gastrointestinal tract, for endpoints with no data, such as DART, the CIR Expert Panel should be asked if information on ascorbic acid should be added to this report.

Additional Considerations

Cosmetic Use - As there are two ingredients in this report "this ingredient" should be changed to "these ingredients".

Dermal Penetration, In Vitro - In the study from reference 36, was the amount of Ascorbyl Glucoside recovered in the skin stated?

Dermal Penetration, Human - It would be helpful to give values for the increase in urinary ascorbic acid after dermal exposure to Ascorbyl Glucoside and/or to indicate if the increase was statistically significant (reference 37).

Short-Term, Oral - The description in this section does not clearly state that guinea pigs (reference 41) were fed either Ascorbyl Glucoside or ascorbic acid in the diet.

Effect on Melanin Synthesis - Please revise the following phrase as it is more likely that Ascorbyl Glucoside decreased the synthesis of melanin, rather than changed the color of melanin: "indicating that Ascorbyl Glucoside had a sustained effect with respect to lightening the color

of melanin."

Summary - Please see slide 11 of this presentation: https://www.toxicology.org/events/shm/fda/docs/2020/2_Monteiro_SOT_FDA_Dermal_Dec_2019.pdf, that indicates "absorption" represents the amount of chemical in the perfusate (blood stream or receptor fluid), while "penetration" represents the amount of chemical that enters the skin. Based on these definitions, the Summary should be changed to state that Ascorbyl Glucoside penetrated the skin where it was metabolized to ascorbic acid which was absorbed. Ascorbyl Glucoside itself was not "absorbed".

The second HRIPT was not "in the same study". Two different HRIPTs were summarized in the same reference that was provided by industry.

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Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Christina Burnett, Senior Scientific Writer/Analyst, CIR
Date: May 15, 2020
Subject: Supplement - Draft Report of the Safety Assessment of Basic Brown 17

Comments on the Draft Report of the Safety Assessment of Basic Brown 17 as Used in Cosmetics were received from the Personal Care Products Council on March 10, 2020 (*bbrown062020sup_pcpc*). Although these comments are included for your review, please note that changes have not been made to the existing report, which had been prepared for the March meeting. Instead, they will be addressed following the June meeting.

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Memorandum

TO: Bart Heldreth, Ph.D.
Executive Director - Cosmetic Ingredient Review

FROM: Alexandra Kowcz, MS, MBA
Industry Liaison to the CIR Expert Panel

DATE: March 10, 2020

SUBJECT: Draft Report: Safety Assessment of Basic Brown 17 as Used in Cosmetics (draft prepared for the March 16-17, 2020 CIR Expert Panel meeting)

The Personal Care Products Council respectfully submits the following comments on the draft report, Safety Assessment of Basic Brown 17 as Used in Cosmetics.

Key Issue

In the Dermal Penetration section and Summary, it would be helpful if the descriptions of the results of the *in vitro* penetration studies were more specific. Please state how much of the compound was found in the receptor fluid and how much was found in the skin. As indicated in slide 11 of this presentation: https://www.toxicology.org/events/shm/fda/docs/2020/2_Monteiro_SOT_FDA_Dermal_Dec_2019.pdf, "absorption" represents the amount of chemical in the perfusate (or receptor fluid), while "penetration" represents the amount of chemical that enters the skin. It is not clear that these terms are being used correctly in the Dermal Penetration section. It is also not clear what is meant by "dermal availability". Does this represent that amount of Basic Brown 17 that was recovered in the skin? Does it include Basic Brown 17 that was recovered in the receptor fluid?

Additional Considerations

Introduction - It would be helpful to note why studies in the 2004 SCCP opinion were not included in the latter SCCS opinions (the material studied was either of an unknown purity or a lower purity than the material used in the studies in the latter opinions).

Genotoxicity - Please state the route of exposure used in the mouse micronucleus assay.

Summary - The Summary should also state that the decrease in body weight gains in the 90-day feeding study in mice was not dose-related.

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Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Monice M. Fiume MMF
Senior Director, CIR
Date: May 15, 2020
Subject: Supplement -Safety Assessment of Caprylhydroxamic Acid as Used in Cosmetics

Comments on the Draft Tentative Report of the Safety Assessment of Caprylhydroxamic Acid as Used in Cosmetics were received from the Personal Care Products Council on March 10, 2020 (*caphyd062020sup_pcpc*). Although these comments are included for your review, please note that changes have not been made to the existing report, which had been prepared for the March meeting. Instead, they will be addressed following the June meeting.

Personal Care Products Council
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Memorandum

TO: Bart Heldreth, Ph.D.
Executive Director - Cosmetic Ingredient Review

FROM: Alexandra Kowcz, MS, MBA
Industry Liaison to the CIR Expert Panel

DATE: March 10, 2020

SUBJECT: Draft Tentative Report: Safety Assessment of Caprylhydroxamic Acid as Used in Cosmetics (draft prepared for the March 16-17, 2020 CIR Expert Panel meeting)

The Personal Care Products Council respectfully submits the following comments on the draft tentative report, Safety Assessment of Caprylhydroxamic Acid as Used in Cosmetics.

Nitrosation - The nitrosamide structure in the text is not correct. There should be a single bond between the two nitrogens and a double bound between the nitrogen and the oxygen.

Cosmetic Use - Presenting the Mintel information (reference 13) in the Cosmetic Use section implies that the new products containing Caprylhydroxamic Acid were cosmetic products. Reference 13 does not indicate the type of product. The Mintel database includes more than just cosmetics and personal care products.

Quantitative Risk Assessment (QRA) - In the paragraph describing MOS determinations, rather than stating "appropriate sensitization assessment factors", it would be clearer to state: "product category based sensitization assessment factors".

Summary - Please revise the statement in the Summary describing how the NESIL was determined. The Summary currently states: "The results of several HRIPTs were used to calculate a WoE NESIL of 1056 μg/cm^2." Although several HRIPTs were considered, the QRA section states: "the highest concentration [should be dose/cm^2] tested in which no positive responses were observed (no-observable-effect-level; NOEL) was 1055.6 μg/cm^2; the lowest-observable-effect-level (LOEL) was 2111.1 μg/cm^2. Therefore, a WoE NESIL of 1056 μg/cm^2 was chosen." The Summary should be revised to indicate that the NESIL was the highest dose/cm^2 that did not cause any sensitization.

Discussion - As the CIR Expert Panel discussed the effect of structure on inhibition of enzymes, in the first paragraph of the Discussion, please revise the second sentence and the beginning of the

first third sentence to: “The Panel noted that the hydroxamic acids known for inhibiting metalloproteinase enzymes through a chelating mechanism do not have a straight chain alkyl group. Because Caprylhydroxamic Acid has a straight alkyl chain....”

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Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Preethi S. Raj
Senior Scientific Analyst/Writer, CIR
Date: May 15, 2020
Subject: Supplement - Safety Assessment of Glycerin Ethoxylates as Used in Cosmetics

Comments on the Draft Tentative Report of the Safety Assessment of Glycerin Ethoxylates as Used in Cosmetics were received from the Personal Care Products Council on March 10, 2020 (*glyeth062020sup_pcpc*). Although these comments are included for your review, please note that changes have not been made to the existing report, which had been prepared for the March meeting. Instead, they will be addressed following the June meeting.

Personal Care Products Council
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Memorandum

TO: Bart Heldreth, Ph.D.
Executive Director - Cosmetic Ingredient Review

FROM: Alexandra Kowcz, MS, MBA
Industry Liaison to the CIR Expert Panel

DATE: March 10, 2020

SUBJECT: Draft Tentative Report: Safety Assessment of Glycerin Ethoxylates as Used in Cosmetics (draft prepared for the March 16-17, 2020 CIR Expert Panel meeting)

The Personal Care Products Council respectfully submits the following comments on the draft report, Safety Assessment of Glycerin Ethoxylates as Used in Cosmetics.

Key Issue

Sensitization, Human, Glycereth-26; Summary - It needs to be clearly stated that the material tested in reference 22 was a 10% aqueous solution of Glycereth-26. This is important because all of the other HRIPTs are on finished products for which only a small part was Glycereth-26. Therefore, in the studies with some dermal observations, it is not known what material in the finished product is responsible for the observed effects.

Additional Considerations

Introduction - In the Introduction it is misleading to state that it is not known how the substances being tested in the studies in the ECHA dossier compare to the cosmetic ingredients. The Chemistry section says the dossier concerns compounds with an average ethoxylation value between 1 and 6.5.

Impurities, Glycereth-26 - "ethylene dioxide" needs to be corrected to "ethylene oxide"

The chemical properties (acid value, hydroxyl value, specific gravity and pH) of Glycereth-26 belong in the Physical and Chemical Properties section, not the Impurities section. They are correctly presented in Table 2.

DART - It is misleading to state that the NOAEL was "because reduction of body weight was observed with females at the highest dose group" as the next sentence indicates that the "weight loss was

considered to be a non-adverse treatment-related effect". It would be clearer to state that the "NOAEL was 1000 mg/kg (the highest dose tested) because the slight body weight decreases at this dose were considered to be non-adverse."

Table 4 - With the exception of the last oral study in Table 4, the dose is given in the first column. Either dose should be added to the heading, or the dose should only be stated in the Dose/Protocol column.

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Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Priya Cherian, Scientific Writer/Analyst, CIR
Date: May 15, 2020
Subject: Supplement - Safety Assessment of Honey-Derived Ingredients as Used in Cosmetics

Comments on the Draft Final Report of the Safety Assessment of Honey-Derived Ingredients as Used in Cosmetics were received from the Personal Care Products Council on March 10, 2020 (*honey062020sup_pcpc*). Although these comments are included for your review, please note that changes have not been made to the existing report, which had been prepared for the March meeting. Instead, they will be addressed following the June meeting.

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Memorandum

TO: Bart Heldreth, Ph.D.
Executive Director - Cosmetic Ingredient Review

FROM: Alexandra Kowcz, MS, MBA
Industry Liaison to the CIR Expert Panel

DATE: March 10, 2020

SUBJECT: Draft Final Report: Safety Assessment of Honey-Derived Ingredients as Used in Cosmetics (draft prepared for the March 16-17, 2020 CIR Expert Panel meeting)

The Personal Care Products Council respectfully submits the following comments on the draft final report, Safety Assessment of Honey-Derived Ingredients as Used in Cosmetics.

Key Issue

The CIR report on Honey ingredients includes a study of aerosolized tualang honey (reference 51) and a nasal irrigation study of manuka honey (reference 51). It would be helpful if these studies were mentioned in the Discussion to support the respiratory tract safety of Honey. The lack of toxicological concerns of Honey exposure to the nasopharyngeal or bronchial regions of the respiratory tract should be based on available data not just "the chemical and biological properties of these ingredients" as currently stated in the Discussion.

Additional Considerations

Impurities - Please check reference 38 (link provided below). Regarding HMF this reference states: "The hydroxymethylfurfural content of honey after processing and/or blending shall not be more than 40 mg/kg. However, in the case of honey of declared origin from countries or regions with tropical ambient temperatures, and blends of these honeys, the HMF content shall not be more than 80 mg/kg."

Summary - The description of the study in which male offspring of treated dams were studied, still states: "treated animals compared to control animals". This should be revised to make it clear that it was male offspring of treated animals that were studied

The description of the study of aerosolized honey in rabbits in the Summary does not make sense without the mention of the pretreatment with ovalbumin to cause inflammation. The ovalbumin exposure needs to be mentioned in the Summary.

Discussion - It should be stated that Honey Powder used in food has been reported to contain fillers.

Reference 38 - As this reference was amended in 2019 (see http://www.fao.org/fao-who-codexalimentarius/sh-proxy/en/?lnk=1&url=https%253A%252F%252Fworkspace.fao.org%252Fsites%252Fcodex%252FStandards%252FCXS%2B12-1981%252FCXS_012e.pdf), it would be more appropriate to use 2019 rather than 1981 in the reference. Please correct WHOW.

Concentration of Use by FDA Product Category – Hexyl Methicone and Simethicone*

Ingredient	Product Category	Maximum Concentration of Use
Simethicone	Other baby products	0.0025%
Simethicone	Other bath preparations	0.0015%
Simethicone	Eyebrow pencils	0.1%
Simethicone	Eyeliners	0.05-0.25%
Simethicone	Eye shadows	0.05-0.052%
Simethicone	Eye lotions	0.004%
Simethicone	Eye makeup removers	0.005%
Simethicone	Mascara	0.005-0.3%
Simethicone	Other eye makeup preparations	0.01-0.16%
Simethicone	Tonics, dressings and other hair grooming aids	0.0013%
Simethicone	Other hair preparations (noncoloring) Rinse-off	0.3% 0.015%
Simethicone	Hair bleaches	0.011%
Simethicone	Face powders	0.05%
Simethicone	Foundations	0.01-0.1%
Simethicone	Lipstick	0.2%
Simethicone	Makeup bases	0.1%
Simethicone	Other makeup preparations	0.0095-0.083%
Simethicone	Basecoats and undercoats (manicuring preparations)	0.005%
Simethicone	Nail polish and enamel	0.1%
Simethicone	Other manicuring preparations Rinse-off Leave-on	 0.01% 0.001%
Simethicone	Bath soaps and detergents	0.01%
Simethicone	Deodorants Not spray Wipe	 0.001% 0.3%
Simethicone	Other personal cleanliness products	0.0000084%
Simethicone	Shaving cream	0.000012%
Simethicone	Shaving soap	0.0000084%
Simethicone	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.000006-0.01%
Simethicone	Face and neck products Not spray	 0.0005-0.048%
Simethicone	Body and hand products Not spray	 0.0074-0.01%
Simethicone	Foot powders and sprays	0.01%
Simethicone	Night products Not spray	 0.01%
Simethicone	Other skin care preparations Rinse-off	0.013-0.2% 0.01%

*Ingredients included in the title of the table but not found in the table were included in the concentration of use survey, but no uses were reported.

Information collected in 2020
Table prepared: April 7, 2020

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Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Preethi S. Raj
Senior Scientific Analyst/Writer, CIR
Date: May 15, 2020
Subject: Supplement -Safety Assessment of Dimethicone, Methicone, and Substituted Methicone Polymers as Used in Cosmetics

Comments on the Draft Amended Report of the Safety Assessment of Dimethicone, Methicone, and Substituted Methicone Polymers as Used in Cosmetics were received from the Personal Care Products Council on March 10, 2020 (*methic062020sup_pcpc*). Also, concentration of use data were received for Hexyl Methicone, and Simethicone, an ingredient being considered for addition, on April 7, 2020 (*methic062020sup_data*). There are no reported concentrations of use for Hexyl Methicone. Simethicone is reported to be used at a maximum concentration of 0.3% (in mascara, deodorant wipes, and "other" hair coloring preparations); the use table data for Simethicone are attached (*methic062020sup_simethicone use*). Although these comments and data are included for your review, please note that changes have not been made to the existing report, which had been prepared for the March meeting. Instead, they will be addressed following the June meeting.

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Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

TO: Bart Heldreth, Ph.D.
Executive Director - Cosmetic Ingredient Review

FROM: Alexandra Kowcz, MS, MBA
Industry Liaison to the CIR Expert Panel

DATE: March 10, 2020

SUBJECT: Draft Amended Report: Safety Assessment of Dimethicone, Methicone, and Substituted Methicone Polymers as Used in Cosmetics (draft prepared for the March 16-17, 2020 CIR Expert Panel meeting)

The Personal Care Products Council respectfully submits the following comments on the draft amended report, Safety Assessment of Dimethicone, Methicone, and Substituted Methicone Polymers as Used in Cosmetics.

Key Issue

The limits for the ingredients included in this report need to be more clearly defined. What are the limitations of the "other substituents", e.g., carbon chain length, saturation, other molecules other than carbon. In the Definition section it states: "The remaining ingredients in this report have 1 or 2 of the substituents on the silicone atoms replaced with alternative functional group." It is not clear what this means. These ingredients are polymers, the value of x (the number of repeating units) is not defined. The substituent maybe on multiple repeating units of the polymer, e.g., the definition of Vinyl Dimethicone says "where some of the methyl groups have been replaced with vinyl groups. The vinyl groups can occur at the ends of the siloxane chain or pendant to the siloxane chain." Some of the ingredients contain nitrogen. Are there any limits as to the nitrogen structures these ingredients may contain?

Additional Considerations

Cosmetic Use - As there is more than one ingredient in this report, "ingredient" needs to be corrected to "ingredients" in several places in the first paragraph of the Cosmetic Use section.

Please state the specific FDA product categories with the maximum use concentrations (as

these cannot be identified in Table 2 and exposure differs depending on the type of product).

Dermal Penetration - Since the study cited to reference 14 did not actually measure levels of Dimethicone in the skin, it does not belong in the dermal penetration section. The *in vitro* absorption study in human skin and vaginal tissue should be moved to the Dermal Penetration section.

ADME, Human, Dimethicone - As the study described in reference 13 did not measure Dimethicone in the blood, "suggesting dermal absorption" should be changed to "suggesting dermal penetration". Please see slide 11 of this presentation: https://www.toxicology.org/events/shm/fda/docs/2020/2_Monteiro_SOT_FDA_Dermal_Dec_2019.pdf, that defines "absorption" as the amount of chemical in the perfusate (blood stream or receptor fluid), while "penetration" represents the amount of chemical that enters the skin.

Acute, Inhalation, old report summary - What concentrations/doses of Methicone and Vinyl Dimethicone were used in the acute inhalation studies in rats? What were the durations (hours of exposure) of these studies?

Acute, Inhalation, Dimethicone - How long were the rats exposed in the study using Dimethicone with an MMPS up to 1.8 µm?

Subchronic, Oral, old report summary - At what doses were changes in body weight or spleen weight observed in rat studies?

DART, old report summary - At what dose of Dimethicone were effects on testes and seminal vesicle weight observed? What were the highest doses that caused no developmental effects? What was the route(s) of exposure used in the DART studies?

Carcinogenicity, old report study - As it states that mice were treated with 50 µl undiluted Dimethicone, it does not make sense to state "an unspecified amount". Perhaps the purity of the Dimethicone was not stated.

Sensitization, old report summary - The following sentence needs to be moved to the Irritation section: "Vinyl Dimethicone was not irritating to rabbits following a 4-hr exposure."

Mucous Membrane Irritation, Dimethicone - What was the range of pH values of the 5 samples of Dimethicone that were tested (reference 18)?

Summary - What compound was tested in the study in which Sprague-Dawley rats were given a single oral dose of 2000 mg/kg bw in corn oil?

What was the route of exposure for the 24-month Dimethicone study in rats (doses of 100, 300 or 1000 mg/kg bw/day)?

What concentration of C30-45 Alkyl Dimethicone was tested in the rabbit irritation study?
What concentration of Dimethicone was tested in the HRIPT in 106 subjects?

Frequency (2020)[1] and concentration (2020)[2] of use of Simethicone

	# of Uses[1]	Max Conc of Use (%)[2]
Totals*	**519**	**0.000006-0.3**
Duration of Use		
Leave-On	*398*	*0.0005-0.3*
Rinse-Off	*120*	*0.000006-0.011*
Diluted for (Bath) Use	*1*	*0.0015*
Exposure Type		
Eye Area	238	0.004-0.3
Incidental Ingestion	32	0.2
Incidental Inhalation-Spray	2; 38[a]; 15[b]	0.0013[a]; 0.01[b]
Incidental Inhalation-Powder	2; 15[b]	0.05; 0.01[b]; 0.0005-0.048[c]
Dermal Contact	161	0.000006-0.3
Deodorant (underarm)	26[a]	Not spray: 0.001; 0.3**
Hair - Non-Coloring	26	0.0013-0.3
Hair-Coloring	103	0.011
Nail	5	0.001-0.1
Mucous Membrane	37	0.0000084-0.2
Baby Products	1	0.0025

*Because this ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure types may not equal the sum of total uses.

**use at this concentration is described for wipes.

[a] It is possible these products are sprays, but it is not specified whether the reported uses are sprays.

[b] Not specified whether a spray or a powder, but it is possible the use can be as a spray or a powder, therefore the information is captured in both categories.

[c] It is possible these products are powders, but it is not specified whether the reported uses are powders

References

1. U.S. Food and Drug Administration (FDA). 2020. U.S. Food and Drug Administration Center for Food Safety & Applied Nutrition (CFSAN). Voluntary Cosmetic Registration Program - Frequency of Use of Cosmetic Ingredients. (Obtained under the Freedom of Information Act from CFSAN; requested as "Frequency of Use Data" January 6, 2020; received January 13, 2020.)

2. Personal Care Products Council. 2020. Concentration of Use by FDA Product Category: Hexyl Methicone and Simethicone. (Unpublished data submitted by Personal Care Products Council on April 7, 2020.)

Commitment & Credibility since 1976

Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Christina Burnett, Senior Scientific Writer/Analyst, CIR
Date: May 15, 2020
Subject: Supplement - Draft Amended Report of the Safety Assessment of Methylisothiazolinone

Comments on the Draft Amended Report of the Safety Assessment of Methylisothiazolinone as Used in Cosmetics were received from the Personal Care Products Council on March 10, 2020 (*MI062020sup_pcpc*). Although these comments are included for your review, please note that changes have not been made to the existing report, which had been prepared for the March meeting. Instead, they will be addressed following the June meeting.

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

TO: Bart Heldreth, Ph.D.
Executive Director - Cosmetic Ingredient Review

FROM: Alexandra Kowcz, MS, MBA
Industry Liaison to the CIR Expert Panel

DATE: March 10, 2020

SUBJECT: Draft Amended Report: Safety Assessment of Methylisothiazolinone as Used in Cosmetics (draft prepared for the March 16-17, 2020 CIR Expert Panel meeting)

The Personal Care Products Council respectfully submits the following comments on the draft amended report, Safety Assessment of Methylisothiazolinone as Used in Cosmetics.

Key Issues

As the CIR Expert Panel was concerned about inhalation safety, it would have been helpful to include a summary of inhalation data from the MCI/MI report including estimates of exposure concentrations of MI.

The FDA VCRP does not distinguish between MI used with MCI and MI used alone. The CIR report should clearly state how the VCRP numbers for MI alone were obtained (it is assumed they were obtained by subtracting reported uses of MCI from the total MI reported uses).

Additional Considerations

Ocular Irritation, Human - Please revise the following sentence (the word "received" is not needed twice): "In an ocular irritation study, 12 human subjects received 100 ppm Methylisothiazolinone in buffered physiological saline received a single 10 µl drop in the eye on 5 consecutive days."

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Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Wilbur Johnson, Jr.
Senior Scientific Analyst, CIR
Date: May 15, 2020
Subject: Supplement - Safety Assessment of Palm Tree-Derived Ingredients as Used in Cosmetics

Comments on the Draft Final Report of the Safety Assessment of Palm Tree-Derived Ingredients as Used in Cosmetics were received from the Personal Care Products Council on March 10, 2020 (*palmtr062020sup_pcpc*). Although these comments are included for your review, please note that changes have not been made to the existing report, which had been prepared for the March meeting. Instead, they will be addressed following the June meeting.

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

TO: Bart Heldreth, Ph.D.
Executive Director - Cosmetic Ingredient Review

FROM: Alexandra Kowcz, MS, MBA
Industry Liaison to the CIR Expert Panel

DATE: March 10, 2020

SUBJECT: Draft Final Report: Safety Assessment of Palm Tree (açai and juçara)-Derived Ingredients as Used in Cosmetics (draft prepared for the March 16-17, 2020 CIR Expert Panel meeting)

The Personal Care Products Council respectfully submits the following comments on the draft final report, Safety Assessment of Palm Tree (açai and juçara)-Derived Ingredients as Used in Cosmetics.

Abstract; Conclusion - The meaning of "intended conditions of use" for Euterpe Oleracea Palm Heart Extract is not clear.

Non-Cosmetic Use - The new sentence cited to reference 42 does not describe a non-cosmetic use. Other than being used in the study described in reference 42, did the authors indicate that this extract has a use?

Anti-Carcinogenicity, Euterpe Oleracea Pulp Powder - In the following sentence, it is not necessary to state "(n = 5 mice per group)" twice. "Some mice from groups 1 to 3 and all mice from group 4 (n = 5 mice per group) were killed 24 h after the first injection of AOM at week 3 (n = 5 mice/group) and liver samples were collected for immunohistochemical and glutathione analysis."

Summary - Please include doses in the paragraph concerning *in vivo* genotoxicity tests.

Discussion - As all the composition data are on fruit, it would be helpful to add the word fruit in the last sentence of the first paragraph as follows: "the Panel agreed that the available data indicate that the composition of the fruit from the two species are similar."

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Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Priya Cherian, Scientific Writer/Analyst, CIR
Date: May 15, 2020
Subject: Supplement - Safety Assessment of Papaya-Derived Ingredients as Used in Cosmetics

Comments on the Draft Report of the Safety Assessment of Papaya-Derived Ingredients as Used in Cosmetics were received from the Personal Care Products Council on March 10, 2020 (*papaya062020sup_pcpc*). Although these comments are included for your review, please note that changes have not been made to the existing report, which had been prepared for the March meeting. Instead, they will be addressed following the June meeting.

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

TO: Bart Heldreth, Ph.D.
Executive Director - Cosmetic Ingredient Review

FROM: Alexandra Kowcz, MS, MBA
Industry Liaison to the CIR Expert Panel

DATE: March 10, 2020

SUBJECT: Draft Report: Safety Assessment of *Carica papaya* (Papaya)-Derived Ingredients as Used in Cosmetics (draft prepared for the March 16-17, 2020 CIR Expert Panel meeting)

The Personal Care Products Council respectfully submits the following comments on the draft report, Safety Assessment of *Carica papaya* (Papaya)-Derived Ingredients as Used in Cosmetics.

Method of Manufacturing - Suppliers of cosmetic ingredients provided two methods of manufacture for Carica Papaya (Papaya) Fruit Extract, and the Dictionary identifies the general method of manufacture for Carica Papaya (Papaya) Fruit Water. This section also includes two methods of manufacture from published papers on papaya leaf extracts. A total of five methods of manufacture are described in this section; three concern cosmetic ingredients, two concern leaf extracts for which the use is not stated. Therefore, the following statement in the introduction to this section is not correct and needs to be revised: "The majority of the methods below are general to the processing of *Carica papaya*, and it is unknown if they apply to cosmetic ingredient manufacturing."

Cosmetic Use - Please state the specific FDA cosmetic product categories associated with the maximum use concentrations.

Acute - The use of "up to" a specific dose suggests lower doses were tested in addition to the highest dose. Based on the information in Table 5, this is correct for all the studies summarized in this section except for the study in rats in which the LD_{50} was reported to be greater than 2000 mg/kg. Only one dose of a leaf extract was given in this study. Please delete "up to" when describing this study.

Short-Term and Chronic - In the text, please also state the doses that were not associated with any adverse effects.

Table 6 - The heading of the first column should include “Dose” rather than “Concentration”, because the values in the column are all mg/kg bw doses.

In which dose group(s) were the SGOT levels significantly increased compared to controls (reference 41)?

References - For unpublished information provided by PCPC, such as references 8 and 9, the following still needs to be added “(Unpublished data submitted by the Personal Care Products Council on [date])”.

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

TO: Bart Heldreth, Ph.D.
Executive Director - Cosmetic Ingredient Review

FROM: Carol Eisenmann, Ph.D.
Personal Care Products Council

DATE: March 30, 2020

SUBJECT: Punica Granatum Flower Extract

Anonymous. 2019. Repeated Insult Patch Test of a Product Containing 0.4% Punica Granatum Flower Extract.

[redacted]

FINAL REPORT

CLIENT: [redacted]

ATTENTION: [redacted]

TEST: Repeated Insult Patch Test
Protocol No.: [redacted]
Protocol Date: [redacted]

TEST MATERIAL: [redacted]
Impressive Formula# [redacted]

Product contains 0.4% Punica Granatum Flower Extract

STUDY NUMBER: [redacted]

Reviewed by: [redacted]

Approved by:

Approved by:

[redacted]

[redacted]

QUALITY ASSURANCE UNIT STATEMENT

Study Number: [redacted]

[redacted] Quality Assurance Unit (QAU) is responsible for auditing the conduct, content and reporting of all clinical trials that are conducted at [redacted]

This trial has been conducted in accordance with the Declaration of Helsinki, the ICH Guideline E6 for *Good Clinical Practice*, the requirements of 21 CFR Parts 50 and 56, other applicable laws and regulations, CPTC Standard Operating Procedures, and the approved protocol.

The [redacted] QAU has reviewed all data, records, and documents relating to this trial and also this Final Report. The following QAU representative signature certifies that all data, records, and documents relating to this trial and also this Final Report have been reviewed and are deemed to be acceptable, and that the trial conforms to all of the requirements as indicated above.

All records and documents pertaining to the conduct of this trial shall be retained in the [redacted] archives for a minimum of ten (10) years. At any time prior to the completion of the tenth archival year, a Sponsor may submit a written request to the [redacted] QAU to obtain custody of trial records once the [redacted] archive period has been completed. This transfer shall be performed at the Sponsor's expense. In the absence of a written request, trial-related records shall be destroyed at the end of the [redacted] archive period with no further notice in a manner that renders them useless.

[redacted]
Quality Assurance Representative

3/27/2019
Date

Objective: To determine by repetitive epidermal contact the potential of a test material to induce primary or cumulative irritation and/or allergic contact sensitization.

Participants: One hundred sixteen (116) qualified subjects, male and female, ranging in age from 16 to 79 years, were selected for this evaluation. One hundred five (105) subjects completed this study. The remaining subjects discontinued their participation for various reasons, none of which were related to the application of the test material.

Inclusion Criteria:

a. Male and female subjects, age 16[a] to 79 years.
b. Absence of any visible skin disease which might be confused with a skin reaction from the test material.
c. Prohibition of use of topical or systemic steroids and/or antihistamines for at least seven days prior to study initiation.
d. Completion of a Medical History Form and the understanding and signing of an Informed Consent Form.
e. Considered reliable and capable of following directions.

Exclusion Criteria:

a. Ill health.
b. Under a doctor's care or taking medication(s) which could influence the outcome of the study.
c. Females who are pregnant or nursing.
d. A history of adverse reactions to cosmetics or other personal care products.

Test Material: [redacted]: Impressive Formula#

Study Schedule:

Panel #	Initiation Date	Completion Date
20190033	January 23, 2019	March 1, 2019
20190035	January 28, 2019	March 8, 2019

[a]With parental or guardian consent

[redacted]

Methodology:

The upper back between the scapulae served as the treatment area. Approximately 0.2 g of the test material, or an amount sufficient to cover the contact surface, was applied to the 3/4" x 3/4" absorbent pad portion of an adhesive dressing. This was then applied to the appropriate treatment site to form an occlusive patch.

Induction Phase:

Patches were applied three (3) times per week (e.g., Monday, Wednesday, and Friday) for a total of nine (9) applications. The site was marked to ensure the continuity of patch application. Following supervised removal and scoring of the first Induction patch, participants were instructed to remove all subsequent Induction patches at home, twenty-four hours after application. The evaluation of this site was made again just prior to re-application. If a participant was unable to report for an assigned test day, one (1) makeup day was permitted. This day was added to the Induction period.

With the exception of the first supervised Induction Patch reading, if any test site exhibited a moderate (2-level) reaction during the Induction Phase, application was moved to an adjacent area. Applications were discontinued for the remainder of this test phase, if a moderate (2-level) reaction was observed on this new test site. Applications would also be discontinued if marked (3-level) or severe (4-level) reactivity was noted.

Rest periods consisted of one day following each Tuesday and Thursday removal, and two days following each Saturday removal.

Challenge Phase:

Approximately two (2) weeks after the final Induction patch application, a Challenge patch was applied to a virgin test site adjacent to the original Induction patch site, following the same procedure described for Induction. The patch was removed and the site scored at the clinic Day 1 and Day 3 post-application.

[redacted]

Methodology (continued):

Evaluation Criteria (Erythema and additional Dermal Sequelae):

0	**=**	**No visible skin reaction**	**E**	**=**	**Edema**
0.5	**=**	**Barely perceptible**	**D**	**=**	**Dryness**
1	**=**	**Mild**	**S**	**=**	**Staining**
2	**=**	**Moderate**	**P**	**=**	**Papules**
3	**=**	**Marked**	**V**	**=**	**Vesicles**
4	**=**	**Severe**	**B**	**=**	**Bullae**
			U	**=**	**Ulceration**
			Sp	**=**	**Spreading**

Erythema was scored numerically according to this key. If present, additional Dermal Sequelae were indicated by the appropriate letter code and a numerical value for severity.

Adverse Events:

On 1/25/19, Subject #23 on Panel 20190033 was admitted to Chilton Hospital in Pequannock, N.J. with stomach pain. A cholecystectomy was conducted on 1/27/19. She was discharged on 1/29/19 and prescribed an antibiotic. She had an uneventful recovery. Since hospitalization was involved, this was considered a serious adverse event. The Principal Investigator judged the severity of this event as life-threatening, but unlikely related to the test material.

Amendments:

There were no amendments.

Deviations:

Owing to inclement weather, Subject #s 37 and 42 on Panel 20190035 missed the 8th Induction Patch.

Due to inclement weather and to a holiday, Subject #s 34, 39, 49, and 60 on Panel 20190035 experienced a delay in the final Induction evaluation of 5 days.

Subject #26 on Panel 20190035 misunderstood directions and returned several days later for the final Induction observation.

The PI judged these deviations to have no impact on clinical trial results.

Results: The results of each participant are appended (Table 1).

Observations remained negative throughout the test interval.

Subject demographics are presented in Table 2.

Protocol is appended.

Summary: Under the conditions of this study, test material, [redacted] Impressive Formula# [redacted], indicated no potential for dermal irritation or allergic contact sensitization.

[redacted]

[redacted]

Table 1
Panel #20190033

Individual Results

[redacted]: Impressive Formula# [redacted]

Subject Number	Day1*	Induction Phase 1	2	3	4	5	6	7	8	9	Virgin Challenge Site Day 1*	Day 3
1	0	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0	0	0	0	0	0
7	0	0	0	0	0	0	0	0	0	0	0	0
8	0	0	0	0	0	0	0	0	0	0	0	0
9	0	0	0	0	0	0	0	0	0	0	0	0
10	0	0	0	0	0	0	0	0	0	0	0	0
11	0	0	0	0	0	0	0	0	0	0	0	0
12	0	0	0	0	0	0	0	0	0	0	0	0
13	0	0	0	0	0	0	0	0	0	0	0	0
14	0	0	0	0	0	0	0	0	0	0	0	0
15	0	0	0	0	0	0	0	0	0	0	0	0
16	0	----------DID NOT COMPLETE STUDY----------										
17	0	0	0	0	0	0	0	0	0	0	0	0
18	0	0	0	0	0	0	0	0	0	0	0	0
19	0	0	0	0	0	0	0	0	0	0	0	0
20	0	0	0	0	0[m]	----------DID NOT COMPLETE STUDY----------						
21	0	0	0	0	0	0	0	0	0	0	0	0
22	0	0	0	0	0	0	0	0	0	0	0	0
23	0	0	----------DID NOT COMPLETE STUDY----------									
24	----------DID NOT COMPLETE STUDY----------											
25	0	0	----------DID NOT COMPLETE STUDY----------									
26	0	0	0	0	0	0	0	0	0	0	0	0
27	0	0	0	0	0	0	0	0	0	0	0	0
28	0	0	0	0	0	0	0	0	0	0	0	0
29	0	0	0	0	0	0	0	0	0	0	0	0

Day 1* = Supervised removal
m = Additional makeup day granted at the discretion of the clinic supervisor

[redacted]

Table 1
(continued)
Panel #20190033

Individual Results

[redacted] Impressive Formula# [redacted]

Subject Number	Day1*	Induction Phase 1	2	3	4	5	6	7	8	9	Virgin Challenge Site Day 1*	Day 3
30	0	0	0	0	0	0	0	0	0	0	0	0
31	0	0	0	0	0	0	0	0	0	0	0	0
32	0	0	0	0	0	0	0	0	0	0	0	0
33	0	0	0	0	0	0	0	0	0	0	0	0
34	0	0	0	0	0	0	0	0	0	0	0	0
35	0	0	0	0	0	0	0	0	0	0	0	0
36	0	0	0	0	0	0	0	0	0	0	0	0
37	0	0	0	0	0	0	0	0	0	0	0	0
38	0	0	0	0	0	0	0	0	0	0	0	0
39	0	0	0	0	0	0	0	0	0	0	0	0
40	0	0	0	0	0	0	0	0	0	0	0	0
41	0	0	0	0	0	0	0	0	0	0	0	0
42	-†	0	0	0	0	0	0	0	0	0	0	0
43	0	0	0	0	0	0	0	0	0	0	0	0
44	0	0	0	0	0	0	0	0	0	0	0	0
45	0	0	0	0	0	0	0	0	0	0	0	0
46	0	0	0	0	0	0	0	0	0	0	0	0
47	0	0	0	0	0	0	0	0	0	0	0	0
48	0	0	0	0	0	0	0	0	0	0	0	0
49	0	0	0	0	0	0	0	0	0	0	0	0
50	0	0	0	0	0	0	0	0	0	0	0	0
51	0	0	0	0	0	0	0	0	0	0	0	0
52	0	0	0	0	0	0	0	0	0	0	0	0
53	0	0	0	0	0	0	0	0	0	0	0	0
54	0	0	0	0	0	0	0	0	0	0	0	0
55	0	0	0	0	0	0	0	0	0	0	0	0
56	0	0	0	0	0	0	0	0	0	0	0	0

Day 1* = Supervised removal
† = Unsupervised removal

[redacted]

[redacted]

Table 1
(continued)
Panel #20190035

Individual Results

[redacted] Impressive Formula# [redacted]

Subject Number	Day1*	Induction Phase 1	2	3	4	5	6	7	8	9	Virgin Challenge Site Day 1*	Day 3
1	0	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
5	----------DID NOT COMPLETE STUDY----------											
6	0	0	0	0	0	0	0	0	0	0	0	0
7	0	0	0	0	0	0	0	0	0	0	0	0
8	0	0	0	0	0	0	0	0	0	0	0	0
9	0	0	0	0	0	0	0	0	0	0	0	0
10	0	0	0	0	0	0	0	0	0	0	0	0
11	0	0	0	0	0	0	0	0	0	0	0	0
12	0	0	0	0	0	0	0	0	0	0	0	0
13	0	0	0	0	0	0	0	0	0	0	0	0
14	0	0	0	0	0	0	0	0	0	0	0	0
15	0	0	0	0	0	0	0	0	0	0	0	0
16	----------DID NOT COMPLETE STUDY----------											
17	0	0	0	0	0	0	0	0	0	0	0	0
18	0	0	0	0	0	0	0	0	0	0	0	0
19	0	0	0	0	0	0	0	0	0	0	0	0
20	0	0	0	0	0	0	0	0	0	0	0	0
21	0	0	0	0	0	0	0	0	0	0	0	0
22	0	0	0	0	0	0	0	0	0	0	0	0
23	0	0	0	0	0	0	0	0	0	0	0	0
24	0	0	0	0	0	0	0	0	0	0	0	0
25	0	0	0	0	0	0	0	0	0	0	0	0
26	0	0	0	0	0	0	0	0	0	0**	0	0
27	0	0	0	0	0	0	0	0	0	0	---DNC---	
28	0	0	0	0	0	0	0	0	0	0	---DNC---	
29	0	0	0	0	0	0	0	0	0	0	0	0

Day 1* = Supervised removal
DNC = Did not complete study
** = Observation recorded late, per deviation

[redacted]

Table 1
(continued)
Panel #20190035

Individual Results

[redacted] Impressive Formula# [redacted]

Subject Number	Day1*	Induction Phase 1	2	3	4	5	6	7	8	9	Virgin Challenge Site Day 1*	Day 3
30	0	0	0	0	0	0	0	0	0	0	0	0
31	0	0	0	0	0	0	0	0	0	0	0	0
32	0	0	0	0	0	0	0	0	0	0	0	0
33	0	0	0	0	0	0	0	0	0	0	0	0
34	0	0	0	0	0	0	0	0	0	0[w]	0	0
35	0	0	0	0	0	0	0	0	0	0	0	0
36	0	0	0	0	0	0	0	0	0	0	0	0
37	0	0	0	0	0	0	0	0	-[w]	0	---DNC---	
38	0	0	0	0	0	0	0	0	0	0	0	0
39	0	0	0	0	0	0	0	0	0	0[w]	0	0
40	0	0	0	0	0	0	0	0	0	0	0	0
41	0	0	0	0	0	0	0	0	0	0	0	0
42	0	0	0	0	0	0	0	0	-[w]	0	---DNC---	
43	0	0	0	0	0	0	0	0	0	0	0	0
44	0	0	0	0	0	0	0	0	0	0	0	0
45	0	0	0	0	0	0	0	0	0	0	0	0
46	0	0	0	0	0	0	0	0	0	0	0	0
47	0	0	0	0	0	0	0	0	0	0	0	0
48	0	0	0	0	0	0	0	0	0	0	0	0
49	0	0	0	0	0	0	0	0	0	0[w]	0	0
50	0	0	0	0	0	0	0	0	0	0	0	0
51	0	0	0	0	0	0	0	0	0	0	0	0
52	0	0	0	0	0	0	0	0	0	0	0	0
53	0	0	0	0	0	0	0	0	0	0	0	0
54	0	0	0	0	0	0	0	0	0	0	0	0
55	0	0	0	0	0	0	0	0	0	0	0	0
56	0	0	0	0	0	0	0	0	0	0	0	0
57	0	0	0	0	0	0	0	0	0	0	0	0
58	0	0	0	0	0	0	0	0	0	0	0	0
59	0	0	0	0	0	0	0	0	0	0	0	0
60	0	0	0	0	0	0	0	0	0	0[w]	0	0

Day 1* = Supervised removal
DNC = Did not complete study
w = Due to inclement weather, subject was unable to report, per deviation

[redacted]

Table 2
Panel #20190033

Subject Demographics

Subject Number	Initials	Age	Gender
1	BMS	22	F
2	M-V	45	F
3	JEJ	48	F
4	SRT	46	F
5	CLS	29	F
6	TRM	61	M
7	S-F	27	M
8	MTR	58	F
9	AMM	19	F
10	SDW	37	F
11	ADC	20	F
12	MAO	64	F
13	DCS	51	F
14	LAK	54	F
15	SAD	40	F
16	LMI	53	F
17	GHS	79	M
18	JMM	40	F
19	VJW	56	F
20	RAS	57	M
21	G-D	57	F
22	VAS	48	F
23	JES	24	F
24	OKW	21	F
25	TJS	23	M
26	DLR	65	F
27	LJR	39	F
28	A-G	60	F
29	MMF	20	F

[redacted]

Table 2
(continued)
Panel #20190033

Subject Demographics

Subject Number	Initials	Age	Gender
30	BCS	62	F
31	JAF	39	F
32	DAT	54	F
33	JRD	27	M
34	JMC	17	F
35	YJP	52	F
36	R-C	19	F
37	AAJ	48	M
38	MAS	52	F
39	DAH	61	F
40	DLK	26	F
41	DSH	31	M
42	Z-B	60	F
43	DMC	61	F
44	HJS	37	F
45	BCM	22	F
46	RPG	51	F
47	CJM	78	F
48	MAG	72	M
49	DLT	60	F
50	N-V	42	F
51	CES	48	F
52	EAS	64	F
53	DCF	49	F
54	GKV	60	F
55	ELR	36	F
56	A-M	65	F

[redacted]

Table 2
(continued)
Panel #20190035

Subject Demographics

Subject Number	Initials	Age	Gender
1	M-L	60	F
2	PAC	65	F
3	HMC	70	M
4	J-S	39	F
5	E-G	42	M
6	LJH	22	F
7	AHS	54	M
8	GAM	56	F
9	RPR	31	F
10	LZV	60	F
11	ACK	74	F
12	SHD	72	F
13	AJG	70	M
14	F-S	26	M
15	LAC	44	F
16	M-F	66	F
17	FTF	60	M
18	GCP	67	F
19	BAG	60	F
20	QCM	41	F
21	KRG	57	F
22	SSD	35	F
23	HLG	43	M
24	JMB	42	F
25	G-D	65	M
26	LDS	33	F
27	MM	45	F
28	C-M	55	M
29	AAM	72	F

[redacted]

Table 2
(continued)
Panel #20190035

Subject Demographics

Subject Number	Initials	Age	Gender
30	JEV	38	M
31	DMW	60	F
32	MAR	56	F
33	LFS	39	M
34	TYB	57	F
35	A-K	58	F
36	SEW	55	F
37	NAE	21	M
38	MAD	48	F
39	NJM	31	F
40	IGD	59	F
41	DLE	48	F
42	M-A	34	M
43	TAS	44	F
44	EPS	16	F
45	LMB	58	F
46	J-C	58	M
47	LDP	71	F
48	S-L	71	F
49	DCG	65	F
50	J-T	30	F
51	RMS	20	M
52	LMS	51	F
53	PNL	39	F
54	RAG	32	M
55	G-G	46	F
56	M-K	61	F
57	D-M	39	F
58	CTH	38	M
59	HFH	66	F
60	JKG	17	F

[redacted]

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Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Christina Burnett, Senior Scientific Writer/Analyst, CIR
Date: May 15, 2020
Subject: Supplement - Draft Final Safety Assessment of *Punica granatum* (Pomegranate)-Derived Ingredients

Comments on the Draft Final Report of the Safety Assessment of *Punica granatum* (Pomegranate)-Derived Ingredients as Used in Cosmetics were received from the Personal Care Products Council on March 10, 2020 (*pomegr062020sup_pcpc*). Although these comments are included for your review, please note that changes have not been made to the existing report, which had been prepared for the March meeting. Instead, they will be addressed following the June meeting.

Additionally, CIR received an unpublished HRIPT study on a product containing 0.4% Pomegranate Flower Extract (*pomegr062020sup_data*). There were 105 subjects that completed the study. The results indicated that the material was not a dermal irritant or sensitizer.

Personal Care Products Council
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Memorandum

TO: Bart Heldreth, Ph.D.
Executive Director - Cosmetic Ingredient Review

FROM: Alexandra Kowcz, MS, MBA
Industry Liaison to the CIR Expert Panel

DATE: March 10, 2020

SUBJECT: Draft Final Report: Safety Assessment of *Punica granatum* (Pomegranate)-Derived Ingredients as Used in Cosmetics (draft prepared for the March 16-17, 2020 CIR Expert Panel meeting)

The Personal Care Products Council respectfully submits the following comments on the draft final report, Safety Assessment of *Punica granatum* (Pomegranate)-Derived Ingredients as Used in Cosmetics.

Abstract; Conclusion - The meaning of "intended conditions of use" for the insufficient data ingredients is not clear.

Composition/Impurities, Punica Granatum Fruit Extract - It should be indicated that the allergens identified in the EU Cosmetic Regulations are fragrance ingredients. Please do not use "Cosmetic Directive" as the directive was changed to a regulation in 2009.

Discussion - In the paragraph about inhalation exposure, please add that the rats were treated by intranasal injection.

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Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Priya Cherian, Scientific Writer/Analyst, CIR
Date: May 15, 2020
Subject: Supplement - Safety Assessment of Quaternium-18 and Quaternium-18 Bentonite as Used in Cosmetics

Comments on the Draft Amended Report of the Safety Assessment of Quaternium-18 and Quaternium-18 Bentonite as Used in Cosmetics were received from the Personal Care Products Council on March 10, 2020 (*quater062020sup_pcpc*). Although these comments are included for your review, please note that changes have not been made to the existing report, which had been prepared for the March meeting. Instead, they will be addressed following the June meeting.

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

TO: Bart Heldreth, Ph.D.
Executive Director - Cosmetic Ingredient Review

FROM: Alexandra Kowcz, MS, MBA
Industry Liaison to the CIR Expert Panel

DATE: March 10, 2020

SUBJECT: Draft Amended Report: Safety Assessment of Quaternium-18 and Quaternium-18 Bentonite as Used in Cosmetics (draft prepared for the March 16-17, 2020 CIR Expert Panel meeting)

The Personal Care Products Council respectfully submits the following comments on the draft amended report, Safety Assessment of Quaternium-18 and Quaternium-18 Bentonite as Used in Cosmetics.

Key Issue

The Summary is the first place in the report that states the reason why the CIR Expert Panel decided to open the report. As the Summary should only include information that was presented earlier in the report. The reason why the report was opened should also be stated in the Introduction of the CIR report. It would also be helpful to state that the CIR Expert Panel was concerned about the potential for Quaternium-18 Bentonite to contain crystalline silica.

Additional Considerations

Introduction - As there are other types of "clays", please revise: "reaction product of Quaternium-18 with clays" to "reaction product of Quaternium-18 with bentonite" (after bentonite, it could state a type of clay).

Method of Manufacture - The method of manufacture of Quaternium-18 Bentonite described in the original CIR report (in the Chemical Properties section) should be summarized in this report.

Acute, Quaternium-18 Bentonite, old report summary - "Bentonite" needs to be added after "Quaternium-18"

Short-Term, Quaternium-18, old report summary - Please state the dose that did not cause any adverse effects.

Subchronic, Quaternium-18, old report summary - Please indicate that the dogs and rats were fed diets containing 2800 ppm Quaternium-18. It is not sufficient to just state a concentration. This concentration in drinking water would result in a different mg/kg/day dose. If this report is only going to state "No signs of toxicity were observed", please delete "No other details regarding this study were provided" as there are other details in the original CIR report. The original CIR report states the endpoints that were examined to reach the conclusion that there were no signs of toxicity.

Dermal Irritation, Quaternium-18 Bentonite - As it states that the study (reference 20) was completed in rabbits, please delete "(species not specified)".

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Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Wilbur Johnson, Jr.
Senior Scientific Analyst, CIR
Date: May 15, 2020
Subject: Supplement - Safety Assessment of *Scutellaria baicalensis*-Derived Ingredients as Used in Cosmetics

Comments on the Draft Tentative Report of the Safety Assessment of *Scutellaria baicalensis*-Derived Ingredients as Used in Cosmetics were received from the Personal Care Products Council on March 10, 2020 (*scutel062020sup_pcpc*). Although these comments are included for your review, please note that changes have not been made to the existing report, which had been prepared for the March meeting. Instead, they will be addressed following the June meeting.

Personal Care Products Council
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Memorandum

TO: Bart Heldreth, Ph.D.
Executive Director - Cosmetic Ingredient Review

FROM: Alexandra Kowcz, MS, MBA
Industry Liaison to the CIR Expert Panel

DATE: March 10, 2020

SUBJECT: Draft Tentative Report: Safety Assessment of *Scutellaria baicalensis*-Derived Ingredients as Used in Cosmetics (draft prepared for the March 16-17, 2020 CIR Expert Panel meeting)

The Personal Care Products Council respectfully submits the following comments on the draft tentative report, Safety Assessment of *Scutellaria baicalensis*-Derived Ingredients as Used in Cosmetics.

Key Issues

The following paper (complete study at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7004199/pdf/JAT-40-270.pdf) that includes *in vitro* mammalian and *in vivo* genotoxicity tests of a Chinese medicine that includes an aqueous extract of the root of *Scutellaria baicelensis* may help address the CIR Expert Panel's concerns about genotoxicity.

Ji K-Y, Kim KM, Oh J-J, et al. 2020. Assessment of the 4-week repeated-dose oral toxicity and genotoxicity of GHX02. *J Appl Toxicol* 40(2): 270-284.

More details about the material tested (one tablet contains 351 mg of a dried aqueous extract of the root of *Scutellaria baicalensis*) is found in the following paper (complete study at https://bmjopen.bmj.com/content/bmjopen/8/5/e019897.full.pdf).

Lyu YR, Yang W-K, Park SJ, et al. 2018. Efficacy and safety of GHX02 in the treatment of acute bronchitis: protocol of a phase II, double-blind, randomised placebo-controlled trial. *BMJ* Open doi:10.1136/bmjopen-2017-019897.

Discussion - The potential for skin whitening should be handled in a manner similar to the Discussion for the pomegranate-derived ingredients. The CIR Expert Panel should make it clear that the *Scutellaria baicalensis*-derived ingredients should be used in cosmetics in a manner that does not cause depigmentation.

The phototoxicity data in the report should be mentioned in the Discussion. An aqueous extract was negative in a 3T3 neutral red uptake phototoxicity assay and a case did not have a phototoxic reaction to a Scutellaria Baicalensis Extract.

Additional Considerations

Definition - The Definition says that the ingredients are derived "from either the root or the sprout plant parts". It should also state that there is a "whole plant" extract.

Effect on Melanogenesis; Discussion - It should be made clear that no effect on melanogenesis was observed in B16F10 cells cultured with an ethanol extract of *Scutellaria baicalensis* root at a concentration of 7 μg/ml.

Reference 13 - Please correct the spelling of "baicanensis"

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Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Priya Cherian, Scientific Writer/Analyst, CIR
Date: May 15, 2020
Subject: Supplement - Safety Assessment of Soy-Derived Ingredients as Used in Cosmetics

Comments on the Draft Final Report of the Safety Assessment of Soy-Derived Ingredients as Used in Cosmetics were received from the Personal Care Products Council on March 10, 2020 (*soy062020sup_pcpc*). Although these comments are included for your review, please note that changes have not been made to the existing report, which had been prepared for the March meeting. Instead, they will be addressed following the June meeting.

Personal Care Products Council
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Memorandum

TO: Bart Heldreth, Ph.D.
Executive Director - Cosmetic Ingredient Review

FROM: Alexandra Kowcz, MS, MBA
Industry Liaison to the CIR Expert Panel

DATE: March 10, 2020

SUBJECT: Draft Final Report: Safety Assessment of Soy-Derived Ingredients as Used in Cosmetics (draft prepared for the March 16-17, 2020 CIR Expert Panel meeting)

The Personal Care Products Council respectfully submits the following comments on the draft final report, Safety Assessment of Soy-Derived Ingredients as Used in Cosmetics.

Composition, Germ Extract - It should be noted that reference 18 indicates that 40% and 26% represent the sum of isoflavones, while 30% is given as the sum of isoflavone glucosides.

Composition, Soybean Extract - It is not clear why some of the units (reference 21) are given as %, while glucose is listed as g/100 g, which is also %. Is this correct? If the units are g/100 g for glucose, please change to % to be consistent with the units for protein and lipid.

Subchronic, Oral, Glycine Soja (Soybean) Extract - Dietary levels should be called concentrations not doses (reference 45).

Chronic, Oral, Glycine Max (Soybean) Seedcoat Extract - Please revise the following sentence: "The authors considered the no-observed adverse-effect-level (NOAEL) of the 5% black soybean hull extract to be 5074.1 mg/kg bw/day in males and 7617.9 mg/kg bw/day for females in mice." The 5% concentration was the NOAEL. The following sentence would be clearer: "The study authors identified the 5% dietary concentration (5074.1 mg/kg be/day males; 7617.9 mg/kg bw/day females) as the NOAEL for mice."

DART; Summary - Throughout the report, please correct "Sertoli's cells" to "Sertoli cells"

Effect on Cancer Cell Proliferation, Glycine Soja (Soybean) Extract - The last sentence (reference 12) has 8 values for percent inhibition, but only 7 test concentrations. Is the first percent inhibition value for the controls?

Sensitization - The last sentence of the first paragraph is not complete. It states: "The test substance was determined to be"

Summary - Please state that the soy ingredient was given in the diet in the SSF study and the chronic study of raw soy flour (up to 79.7%). Please state the dose of soy flour used in the study in 72 male albino mice.

In the description of the tumor-promotion study of raw soy flour, please indicate that the nodules were observed in the pancreas.

In the estrogenic activity paragraph, please correct: "A reported gene assay" to "A reporter gene assay"

Discussion - The CIR report on soy proteins includes descriptions of the proteins reviewed in the Chemistry section. The current report does not include descriptions of proteins that may be found in these ingredients. In the paragraph in the Discussion about Type I allergy (IgE-mediated) taken from the CIR report on soy proteins it is not clear what is meant by "these cosmetic ingredients". This appears to be referring to proteins as described in soy protein and peptide report, but may be misinterpreted as applying to the ingredients in this report . What is known about the proteins that may be found in the ingredients in this report? It would be helpful if the Discussion stated that proteins in the ingredients in the current report should have molecular weights below that which would cause IgE cross-linking.

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Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Wilbur Johnson, Jr.
Senior Scientific Analyst, CIR
Date: May 15, 2020
Subject: Supplement - Safety Assessment of Sulfites as Used in Cosmetics

Comments on the Draft Amended Report of the Safety Assessment of Sulfites as Used in Cosmetics were received from the Personal Care Products Council on March 10, 2020 (*sulfit062020sup_pcpc*). Although these comments are included for your review, please note that changes have not been made to the existing report, which had been prepared for the March meeting. Instead, they will be addressed following the June meeting.

Personal Care Products Council
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Memorandum

TO: Bart Heldreth, Ph.D.
Executive Director - Cosmetic Ingredient Review

FROM: Alexandra Kowcz, MS, MBA
Industry Liaison to the CIR Expert Panel

DATE: March 10, 2020

SUBJECT: Draft Amended Report: Safety Assessment of Sulfites as Used in Cosmetics (draft prepared for the March 16-17, 2020 CIR Expert Panel meeting)

The Personal Care Products Council respectfully submits the following comments on the draft amended report, Safety Assessment of Sulfites as Used in Cosmetics.

Key Issues

It is not clear why the following study published in 2012 was not included in the CIR report as it seems very relevant.

Roberts DW, Basketter D, Kimber I, et al. 2012. Sodium metabisulfite as a contact allergen - An example of a rare chemical mechanism for protein modification. *Contact Dermatitis* 66(3): 123-127.

Effect on Allergic Pulmonary Sensitization Co-Elicitation; Summary - What dose of Sodium Sulfite was used in this study?

Additional Considerations

Cosmetic Use - As this report concerns more than one ingredient, “this ingredient” in the first paragraph needs to be corrected to “these ingredients”.

Cosmetic Use; Summary - Please name the specific FDA cosmetic product categories in which the highest use concentrations were reported.

ADME, Animal, Oral, old report summary - Please name the ingredient(s).

Subchronic, Oral, Sodium Bisulfite, old report summary - What doses/dietary concentrations were used in the study in mice in which Ehrlich ascites mouse carcinoma cells were implanted?

Chronic, Oral, Sodium Bisulfite, old report summary - It is not clear what is meant by “aged diet”. For how long was the diet aged? What was the fate of the Sodium Bisulfite in the “aged diet”?

In the study of Sodium Bisulfite in mice, did they really not feed the mice at all ("100% of the feed was restricted as an additional stress factor")?

DART, Oral, Sodium Bisulfite, Sodium Metabisulfite, old report summary - Please include the gestation days of treatment for all developmental toxicity studies.

DART, Oral, Sodium Metabisulfite, old report summary - The description of the three generation rat study is not clear. Did they really mate controls with treated groups to get generation II? It currently states: "Likewise, the sulfite drinking water groups of generation II were produced from matings of control groups of generation I." It also states the following which does not make sense: "Generation II was derived similarly from generation II."

DART, Oral, Sodium Metabisulfite; Summary - The title of reference 27 suggests that they looked at whether or not curcumin prevented the testicular effects of Sodium Metabisulfite. Since curcumin is an antioxidant, the interaction study may suggest a mechanism of Sodium Metabisulfite effects. If the interaction study is not added to the CIR report, the following needs to be deleted from the Summary: "A study on protection against Sodium Metabisulfite-induced testicular toxicity was performed."

DART, Oral, Sodium Sulfite, old report study - This summary lists 5 dietary concentrations of Sodium Sulfite for a rat developmental toxicity study, but only 4 doses are listed. It is not clear which dose belongs to which dietary concentration.

Genotoxicity, In Vitro, Sodium Metabisulfite, old report study - The *in vivo* studies, e.g., dominant lethal assay, need to be moved to the *in vivo* subsection.

Genotoxicity, In Vivo - Please state the doses and route of exposure used in the study described in reference 32.

Carcinogenicity, old report summary - The IARC review should be cited to IARC not the original CIR report.

Please state the doses used in the rat studies (described as "at lower doses than in the mouse studies").

Carcinogenicity, Oral, Sodium Bisulfite, old report summary - The following does not make sense: "rats were fed either one or four diets".

Phototoxicity, old report summary - Details of the UV exposure are given for one lamp, they should also be provided for the other two lamps.

Irritation, Sodium Metabisulfite, old report summary - What was the concentration of Sodium Metabisulfite in the solution that was applied to 6 albino rabbits undiluted?

Case Reports - Please use the word petrolatum instead of Vaseline as vaseline® is a registered name.

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Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Preethi S. Raj
Senior Scientific Analyst/Writer, CIR
Date: May 15, 2020
Subject: Supplement - Safety Assessment of Tris(Tetramethylhydroxypiperidinol) Citrate as Used in Cosmetics

Comments on the Draft Report of the Safety Assessment of Tris(Tetramethylhydroxypiperidinol) Citrate as Used in Cosmetics were received from the Personal Care Products Council on March 10, 2020 (*tricit062020sup_pcpc*). Although these comments are included for your review, please note that changes have not been made to the existing report, which had been prepared for the March meeting. Instead, they will be addressed following the June meeting.

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Memorandum

TO: Bart Heldreth, Ph.D.
Executive Director - Cosmetic Ingredient Review

FROM: Alexandra Kowcz, MS, MBA
Industry Liaison to the CIR Expert Panel

DATE: March 10, 2020

SUBJECT: Draft Report: Safety Assessment of Tris(Tetramethylhydroxypiperidinol) Citrate as Used in Cosmetics (draft prepared for the March 16-17, 2020 CIR Expert Panel meeting)

The Personal Care Products Council respectfully submits the following comments on the draft report, Safety Assessment of Tris(Tetramethylhydroxypiperidinol) Citrate as Used in Cosmetics.

Key Issue

The CIR Expert Panel should be asked if it is appropriate to add data on 2,2,4,4-tetramethyl-4-piperidinol –oxide (Tempol; CAS No. 2226-96-2) to the report. Data on the compound without the hydroxyl group (2,2,6,6-tetramethyl-1-piperidinyloxy; Tempo; CAS No. 2564-83-2) may also be helpful. Both of these compounds have ECHA dossiers.

Additional Considerations

Acute, Oral - Please delete “that died” in the following sentence as it does not make sense: “(There was no mortality in the lower dose groups that died.)”

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Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Wilbur Johnson, Jr.
Senior Scientific Analyst, CIR
Date: May 15, 2020
Subject: Supplement - Safety Assessment of Vanilla-Derived Ingredients as Used in Cosmetics

Comments on the Draft Final Report of the Safety Assessment of Vanilla-Derived Ingredients as Used in Cosmetics were received from the Personal Care Products Council on March 10, 2020 (*vanill062020sup_pcpc*). Although these comments are included for your review, please note that changes have not been made to the existing report, which had been prepared for the March meeting. Instead, they will be addressed following the June meeting.

Personal Care Products Council
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Memorandum

TO: Bart Heldreth, Ph.D.
Executive Director - Cosmetic Ingredient Review

FROM: Alexandra Kowcz, MS, MBA
Industry Liaison to the CIR Expert Panel

DATE: March 10, 2020

SUBJECT: Draft Final Report: Safety Assessment of Vanilla-Derived Ingredients as Used in Cosmetics (draft prepared for the March 16-17, 2020 CIR Expert Panel meeting)

The Personal Care Products Council respectfully submits the following comments on the draft final report, Safety Assessment of Vanilla-Derived Ingredients as Used in Cosmetics.

Abstract; Conclusion - It is not clear what is meant by "intended conditions of use" for the insufficient data ingredients.

Composition, *Vanilla planifolia* fruit - Please delete "(units not stated)" as the units for vanillin composition have been added to the report.

Discussion - It would be helpful to identify the constituents of concern before the following sentence as it would clarify what is meant by "these constituents". "Because the final product formulations may contain multiple botanicals, each possibly containing the same constituents of concern, formulators are advised to be aware of these constituents and to avoid reaching levels that may be hazardous to consumers."

There is a lot of information in this report concerning composition of vanilla (6 tables) and little information about "chemical and biological properties". Therefore, in the paragraph on inhalation safety, "chemical and biological properties" should be changed to "composition".

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Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Christina Burnett, Senior Scientific Writer/Analyst, CIR
Date: May 15, 2020
Subject: Supplement - Draft Tentative Report of the Safety Assessment of Wheat-Derived Ingredients

Comments on the Draft Tentative Report of the Safety Assessment of Wheat-Derived Ingredients as Used in Cosmetics were received from the Personal Care Products Council on March 10, 2020 (*wheat062020sup_pcpc*). Although these comments are included for your review, please note that changes have not been made to the existing report, which had been prepared for the March meeting. Instead, they will be addressed following the June meeting.

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

TO: Bart Heldreth, Ph.D.
Executive Director - Cosmetic Ingredient Review

FROM: Alexandra Kowcz, MS, MBA
Industry Liaison to the CIR Expert Panel

DATE: March 10, 2020

SUBJECT: Draft Tentative Report: Safety Assessment of Wheat-Derived Ingredients as Used in Cosmetics (draft prepared for the March 16-17, 2020 CIR Expert Panel meeting)

The Personal Care Products Council respectfully submits the following comments on the draft tentative report, Safety Assessment of Wheat-Derived Ingredients as Used in Cosmetics.

Key Issue

In the memo, it is misleading to state that "none of the requested data have been received". Although no new data were received, an HRIPT on the product with the highest concentration (13% Triticum Vulgare (Wheat) Germ Extract) was already in the report. As the accepted scientific name for *Triticum vulgare* is *Triticum aestivum*, this study should also be sufficient for Triticum Aestivum (Wheat) Germ Extract. An HRIPT of a product containing 2% Wheat Germ Glycerides was in the old report (the new maximum use concentration is 0.2%). Therefore, among the dermal irritation/sensitization data the CIR Expert Panel requested, the only information that is missing is on Triticum Vulgare (Wheat) Sprout Extract.

Additional Considerations

Tumor/Anti-Tumor Promotion, Triticum Vulgare (Wheat) Sprout Extract - It is not clear that the study on wheatgrass extract (also called wheatgrass leaf extract; reference 48) belongs under the subheading, Triticum Vulgare (Wheat) Sprout Extract.

Dermal Sensitization, Animal, Wheat Germ Glycerides, old report summary - As the CIR Expert Panel requested additional sensitization data on Wheat Germ Glycerides, it would be helpful if more details of the guinea pig sensitization study from the original report were included in this summary, e.g., 6 guinea pigs were in each group (treatment and control); all of the exposures were by intracutaneous injection (total of 10 injection 0.05 ml first induction injection and

challenge injection; 0.1 ml 9 induction injections).

Dermal Sensitization, Human, Wheat Germ Glycerides - As the CIR Expert Panel requested additional sensitization data on Wheat Germ Glycerides, it would be helpful if more details of the human sensitization studies from the original report were included in this summary, e.g., a lipstick base containing 2% Wheat Germ Glycerides was tested in 1154 subjects in a modified Draize-Shelanski HRIPT, reactions consistent with irritation were observed in 8 subjects.

Summary - As wheat germ is not an accepted OTC drug for weight control products (it is in CFR 310.545), the Summary should not state: “wheat germ is an OTC weight control drug product.”

Accept for sensitive individuals as suggested in Introduction, wheat in the diet does not cause health problems. Therefore, the Summary should not suggest that oral consumption of wheat has the potential to cause systemic effects.

Discussion - In the Discussion, please state the constituents of concern for wheat. The conclusion from the CIR report on Hydrolyzed Wheat Protein should also be stated in the Discussion and it should indicate that protein components in some of the ingredients in the current report should comply with the same limitations.

As it is not clear what is meant by “chemical and biological properties” of the wheat-derived ingredients, it would be clearer to base inhalation safety on composition.

Reference 48 - Please correct “Chemopreventtion”