Communications Supplement

Acetyl Hexapeptide-8

Adenosine

Benzophenones

Caprylhydroxamic Acid

Coconut

Diacetone Alcohol

Levulinic Acid

Red Algae

Saccharide Humectants

Silicates

Scutellaria

Tetrasodium Glutamate Diacetate

Ubiquinone

EXPERT PANEL MEETING
September 14-15, 2020

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Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Bart Heldreth, PhD, Executive Director, CIR
Date: September 10, 2020
Subject: Communications

Enclosed are communications received on the current CIR reports for this meeting. Please note that no further communications were received for MI, Ascorbyl Glucoside, Polysilicone-11, the rereview summaries, or Priorities.

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: September 4, 2020

SUBJECT: Draft Report: Safety Assessment of Acetyl Hexapeptide-8 and Acetyl Hexapeptide-8 Amide as Used in Cosmetics (draft prepared for the September 14-15, 2020 meeting of the Expert Panel for Cosmetic Ingredient Safety)

The Personal Care Products Council respectfully submits the following comments on the draft report, Safety Assessment of Acetyl Hexapeptide-8 and Acetyl Hexapeptide-8 Amide as Used in Cosmetics.

Dermal Penetration – It is not clear what is meant by n=5 in the following sentence: "Five parallel experiments for each formulation (n = 5) were performed." Because the sentence states that there were 5 experiments, either "(n=5)" should be deleted or changed to "(n=3)" to indicate the number of formulations tested.

Cytotoxicity – It is not clear if the following information in this section is just about the control, Doxorubicin, or if some of these results were for Acetyl Hexapeptide-8 Amide. "Doxorubicin, a commonly used drug in cancer chemotherapy, served as the reference compound. Significant antiproliferative activity was observed at concentrations above 10 µM. Calculated half-maximal inhibitory concentration (IC_{50}) values were 34.862 µM (in HEK-293 cells) and 64.458 (in IMR-32 cells). In human epidermal fibroblasts, a dose-dependent antiproliferative effect was observed; 67% inhibition was observed at 100 µM (highest test concentration). "

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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: September 4, 2020

SUBJECT: Draft Final Report: Safety Assessment of Adenosine Ingredients as Used in Cosmetics (draft prepared for the September 14-15, 2020 meeting of the Expert Panel for Cosmetic Ingredient Safety)

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

Introduction – Please correct “structurally similarities”

Non-Cosmetic Use –The units, mg/ml, is a concentration not a dose as stated in the Non-Cosmetic Use section. Reference 22 actually says that 3 mg/ml is the concentration of Adenosine in the iv- dosing solution. The dose for adults is stated as 140 µg/kg/min infused for 6 minutes for a total dose of 0.84 mg/kg.

Dermal Penetration, Human; Summary - The summary of the Norwegian risk assessment does not make sense as presented in the Dermal Penetration and Summary sections as the units mg/cm^2 is a dose not thickness as stated in the CIR report. The Norwegian risk assessment actually estimated human exposure to Adenosine assuming cosmetic products contained 0.1% Adenosine. Based on SCCS methods, they assumed 2% absorption of Adenosine from cosmetic products (2% absorption was not an outcome of the risk assessment as suggested by the CIR report). They used an application rate of 1 mg/cm^2 (not 2 mg/cm^2 – the value given for thickness in the CIR report). The following conclusion was reached by the Norwegian risk assessment "Adenosine should only be used for anti-aging creams for face and eyes at concentrations up to 0.1% - and not in any other cosmetic products." It is not clear that the summary of the Norwegian risk assessment should be included in the dermal penetration section.

Summary - The Summary should be consistent with what was said earlier "(i.e., 0.075% mannitol and 0.075% Disodium Adenosine Triphosphate) was used for the intracutaneous

induction, and a 10% aqueous dilution of the test substance (i.e., 1.5% mannitol, 1.5% Disodium Adenosine) was used for the epicutaneous induction and challenge". In contrast the Summary states: "(0.075% mannitol and 0.075% Disodium Adenosine Triphosphate (challenge) [this should be intracutaneous induction]; 1.5% mannitol, 1.5% Disodium Adenosine Triphosphate (induction) [this should be epicutaneous induction and challenge)".

Discussion – It would be helpful if the Discussion mentioned the human inhalation data included in the report.

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: September 4, 2020

SUBJECT: Draft Amended Report: Safety Assessment of Benzophenones as Used in Cosmetics (draft prepared for the September 14-15, 2020 meeting of the Expert Panel for Cosmetic Ingredient Safety)

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

Key Issues
It would be helpful if some of the information in the report, such as human biomonitoring data, genotoxicity data and case reports were summarized in tables.

Cosmetic Use; Summary; Table 3 – In the use information (text, Summary and Table 3), please also include cosmetic use information from the re-review (use information is from 2002).

Cosmetic Use – The EU limitation for Benzophenone-3 presented in the cosmetic use section is not correct. It was changed to match the SCCP opinion in 2017 it should be: 6% for sunscreen use; "Other: Not more than 0.5 % to protect product formulation; Wording of conditions of use and warnings: Contains Benzophenone-3".

Other Clinical Reports - With the exception of the summary from the original CIR report and the last study in this section, all of the studies in this section are cross-sectional epidemiology studies and should be moved to the epidemiology section.

Summary – The following statement is not correct: "the SCCP concluded that the use of Benzophenone-3 as a UV filter at concentrations up to 0.5% in all types of cosmetic products does not pose a risk to the health of the consumer, apart from its contact allergenic and photoallergenic potential." The actual conclusion is: ""the use of benzophenone-3 as a UV-filter up to 6% in cosmetic sunscreen products and up to 0.5% in all types of cosmetic products to

protect the formulation does not pose a risk to the health of the consumer, apart from its contact allergenic and photoallergenic potential." The 0.5% limit is to protect the product – not "as a UV filter".

Table 3, Benzophenone-9 – What is the source of the 0.35% use concentration associated with Benzophenone-9? There are no use concentrations reported for Benzophenone-9 in the 2020 concentration of use information provided by PCPC.

Additional Considerations

Memo – The memo states that the re-review summary was published in 1985. This is not correct; the re-review summary was published in 2005. The concentration of use information in the published re-review summary is from 2002.

Introduction – Please identify the ingredients for which ECHA dossiers are available.

Non-Cosmetic Use – The names of the ingredients when used as sunscreens in the United States should be added to the Non-Cosmetic Use section (Benzophenone-3 [Oxybenzone], Benzophenone-4 [Sulisobenzone], Benzophenone-8 [Dioxybenzone]).

Dermal Penetration, In Vitro, Benzophenone-3 – The Benzophenones studied in reference 22 are not clear. Did they only study Benzophenon-3, or were other Benzophenone ingredients also studied?

Dermal Penetration, In Vitro, Benzophenone-3 – It is not necessary to present reference 24 in both the *in vitro* and *in vivo* subsections. What were the flux values for Benzophenone-3?

Dermal Penetration, In Vitro, Benzophenone-3 – What were the absorption rates for Benzophenone-3 in the different vehicles (reference 25)?

Dermal Penetration, In Vitro, Benzophenone-3 and -4 - What was the limit of detection for Benzophenone-4 (reference 26)?

Dermal Penetration, In Vitro, Benzophenone-3 and -4 – In the study described in reference 27, where was Benzophenone-4 found? in the receptor fluid or in the skin, or both?

Dermal Penetration, Animal, Benzophenone-2 – The study in this subsection (no reference) does not belong in the dermal penetration section as they are studying metabolism rather than dermal penetration. It is not clear how the animals were treated (or if this is an *in vitro* metabolism study).

Dermal Penetration, Human, Benzophenone-3 - It is not necessary to give the results for the compounds other than Benzophenones (reference 23).

Dermal Penetration, Risk Assessment – The Dermal Penetration section does not seem to be the appropriate section for the risk assessment.

Risk Assessment - It is not sufficient to just state the MOS values (reference 25). What were the exposure estimates? What was the toxicity value, e.g., NOAEL, used to calculate the MOS values?

Risk Assessment – Reference 30 belongs in the *in vitro* dermal penetration section. It is not clear why it is presented in the middle of the risk assessment. What were the results of this study?

Risk Assessment – The following paragraph needs a reference and it does not appear to be in the correct location in this report: "The estimated systemic exposure dose of Benzophenone-3 after sunscreen application (at 1 mg/cm^2) for 6 h to the face and whole-body skin was estimated to be 136 mg/cm^2 and 30 mg/cm^2, respectively. Skin shaving increased Benzophenone-3 bioavailability by 1.38-fold. MOS values were estimated according to guidelines applicable for the European Union. For 3 realistic exposure scenarios, MOS values of 48, 34, and 34 for Benzophenone-3 in sunscreen applied to the whole-body indicated some concerns regarding safety for consumers (MOS < 100)."

Risk Assessment – In the description of the SCCP risk assessment, why does the calculation example say 2% formulation when the heading says 0.5%?

ADME, In Vitro, Benzophenone-2 – What are the sources of the following cell lines: MELN and T47D-KBLuc?

ADME, Animal, Dermal, Benzophenone-2 – Please state how long after dermal application for the following observation "the blood level of Benzophenone-2 was ~300 ng/ml" (reference 35)?

ADME, Animal, Oral, Benzophenone-3 – Did reference 39 examine radioactivity levels in tissues in addition to the liver and kidneys?

ADME, Human - Because sunscreen use tends to be seasonal, it would be helpful to note the season samples were collected in the human biomonitoring studies.

ADME, Human, Benzophenone-1, Benzophenone-2, Benzophenone-3, Benzophenone-4 Benzophenone-6, and Benzophenone-8 – The following paragraph cited to reference 49 appears to be describing the same study described in the first paragraph of this section (both paragraphs are cited to reference 49). If it is two different analyses from the same population, they should be presented together. "An exposure assessment on Benzophenones-1, -2, -3, - 4, and 8, conducted from 2010 to 2011, involved a population of 1576 subjects in South Korea. Urine samples were collected. The detection frequency for Benzophenone-1 was above 55.8%, and the detection frequency for Benzophenone-3 was 24.8%. The detection rate for the remaining benzophenones (Benzophenones-2, -4, and -8) was lower than 14%. The geometric mean values of urinary Benzophenone-1 and Benzophenone-3 were 1.24 ng/ml and 2.66 ng/ml, respectively. Concentrations of Benzophenone-2, Benzophenone-4 and Benzophenone-8 in the urine were virtually undetectable."

ADME, Human, Benzophenone-3 – Reference 69 is more appropriately presented in the epidemiology section rather than the ADME section. There is no information presented in the

ADME section to support the following statement – it should be deleted: “They also concluded that there is a direct association of Benzophenone-3 exposure and Hirschsprung’s disease in neonates under normal conditions of use of sunscreen products.”

Acute, Dermal, old report summary - Were the doses applied really greater than 5 g/kg? or were doses of 5 g/kg applied and no deaths observed?

Short-Term Dermal, Benzophenone-3 – It is not clear how long the rats were treated in the study from reference 37.

Subchronic, Oral, old report summary – What were the toxic effects observed in these studies (it would be helpful to at least state the target organs)?

DART, In Vitro, Benzophenone-3; Summary – As whole embryos are used in zebrafish embryo studies, they are generally not considered “in vitro” studies. The Summary calls the zebrafish study “a cell model”, this is not correct as the whole embryo is used.

DART, Animal, Dermal, Benzophenone-3 – What happened to the females (reference 71)?

DART, Animal, Oral, Benzophenone-3 – In the study from reference 42, please identify the organs that had reduced weights.

DART, Animal, Oral, Benzophenone-3; Effects on Gene Expression – Please revise the following sentence (found in more than one place in this report) as it is unlikely that the rats were exposed via milk after weaning, as implied in this sentence. “The male offspring, evaluated in this study, were then weaned on postnatal day 28, and subsequently dosed with Benzophenone-3 via chow and milk.”

DART, Animal, Oral, Benzophenone-12 – In the developmental toxicity study of Benzophenone-12, were there really male rats included in this study? If so, when were the males dosed in relation to mating?

Irritation, Human, Benzophenone-4 – In the description of the study from reference 114, it is not clear if all 80 subjects were tested with all three concentrations of Benzophenone-4.

Sensitization, Human, old report summary – This summary needs to be italicized.

Photosensitization/Phototoxicity, Human, Benzophenone-3 – In the description of reference 120, it should be made clear that this study was based on 7 years of testing. "Since 1990" suggests that this study was done over a longer time period.

Retrospective and Multicenter Studies – Why is the photosensitization study (reference 128) in this section while similar studies are in the Photosensitization/Phototoxicity section?

Summary – The Summary should indicate if the oral studies were dietary, drinking water or gavage studies.

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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: September 9, 2020

SUBJECT: Draft Final Report: Safety Assessment of Caprylhydroxamic Acid as Used in Cosmetics (draft prepared for the September 14-15, 2020 meeting of the Expert Panel for Cosmetic Ingredient Safety)

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

To be consistent with other CIR reports, how the theoretical potential of nitrosamide formation is presented in the CIR report on Caprylhydroxamic Acid should be changed. For example, the CIR report on fatty acid amidopropyl dimethylamines (published in 2019) does not mention nitrosamine formation in the abstract. The Discussion of the report on fatty acid amidopropyl dimethylamines states "the Panel recommended that these ingredients should not be included in cosmetic formulations containing N-nitrosating agents." The theoretical potential of nitrosamide formation should be removed from the abstract on the CIR report on Caprylhydroxamic Acid, and rather than recommending monitoring, the Discussion should state that Caprylhydroxamic Acid should not be including in cosmetic formulations containing N-nitrosating agents. This approach would be consistent with previous CIR reports.

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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: September 9, 2020

SUBJECT: Draft Tentative Report: Safety Assessment of *Cocos nucifera* (Coconut)-Derived Ingredients as Used in Cosmetics (draft prepared for the September 14-15, 2020 meeting of the Expert Panel for Cosmetic Ingredient Safety)

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

Memo – The memo states that PCPC is performing a concentration of use survey on Cocos Nucifera (Coconut) Flower Nectar Extract. This is not true. There has not been a request from CIR staff to complete a concentration of use survey on Cocos Nucifera (Coconut) Flower Nectar Extract.

Introduction; References - Reference 5 is the dossier on the coconut ferment ingredient that was taken out of the report. The Introduction needs to be revised and the reference should be deleted from the reference section.

Table 2, Cocos Nucifera (Coconut) Fruit Extract – There are a number of categories for which the maximum use concentration is listed as 0.4%. It is not clear why the total row indicates a maximum use concentration of 0.2%.

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: September 9, 2020

SUBJECT: Draft Report: Safety Assessment of Diacetone Alcohol as Used in Cosmetics (draft prepared for the September 14-15, 2020 meeting of the Expert Panel for Cosmetic Ingredient Safety)

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

Non-Cosmetic Use – It is not clear that the occupational exposure values should be presented in the Non-Cosmetic Use section. Although OSHA and NIOSH may use the same value (50 ppm), what they represent is different. The OSHA value is a permissible exposure level (PEL) for exposure over an 8-hour work day that is a regulation. The NIOSH value is a recommended exposure level (REL) over a 10-hour work day. The OSHA PEL should be cited to OSHA rather than NIOSH (reference 5).

Sub-chronic, Oral – Please correct: “Sprague-Dawley rats were Diacetone Alcohol in corn oil…” (add “exposed to”)

DART – Reduced “number of live pups at day 4 of lactation, and survival at day 4 of lactation was observed in pups at the 1000 mg/kg bw/d dose level” appears to be saying the same thing two different ways.

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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: September 4, 2020

SUBJECT: Draft Report: Safety Assessment of Levulinic Acid and Sodium Levulinate as Used in Cosmetics (draft prepared for the September 14-15, 2020 meeting of the Expert Panel for Cosmetic Ingredient Safety)

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

Introduction; References - Reference 4, as listed in the reference section, is not a "pre-proof" as stated in the Introduction, it is the reference that was published on the internet before the hard copy of the journal was available.

Method of Manufacture – Please correct the spelling of “poylsaccharides”

Sensitization, In Vitro/In Chemico – As the study included in this section was done in cells, “In Chemico” is not needed in this subheading. Units of µg/ml should be called “concentrations” rather than “doses”.

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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: September 4, 2020

SUBJECT: Draft Report: Safety Assessment of Red Algae-Derived Ingredients as Used in Cosmetics (draft prepared for the September 14-15, 2020 meeting of the Expert Panel for Cosmetic Ingredient Safety)

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

Kappaphycus Alvarezii Extract should be added to this report as it is derived from a red algae species, a supplier has provided some information on a trade name mixture that contains this ingredient, and the concentration of use survey is underway.

Memo – Which of the 59 INCI names includes more than one species of red algae?

Composition/Impurities – The first sentence of this section is cited to reference 8 which the title indicates is about *Gelidium amansii*. Is it appropriate to extend this statement to other species of red algae? Are there other references that include similar statements about the composition of red algae?

Composition/Impurities, Ahnfeltiopsis Concinna – Information about *Chondrus crispus* does not belong in this subsection.

Cosmetic Use – In the Cosmetic Use section, it would be helpful to state the number of ingredients with no reported uses.

Non-Cosmetic Use – In this section, it would be helpful to state the species that are used as food under the name nori as this information is also not presented in Table 12.

Subchronic - What were the differences in organ weights and what organs were affected? Only the statistically significant differences should be mentioned.

Cytotoxicty – What were the highest concentrations tested (reference 59)?

Dermal Irritation – Please state the types of *in vitro* dermal irritation tests that were completed. Please state the ingredients tested in the human irritation tests.

Summary – Please state the type of “radiation” that was used in the study of photoprotective effects.

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: September 4, 2020

SUBJECT: Draft Report: Safety Assessment of Saccharide Humectants as Used in Cosmetics (draft prepared for the September 14-15, 2020 meeting of the Expert Panel for Cosmetic Ingredient Safety)

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

ADME, Oral, Psicose – Please correct: "Of the exhaled [^{14}C]carbon dioxide, 26% was exhaled within 7 h and 80% was inhaled within 24 h." It is likely that "inhaled within 24 h" should be "exhaled within 24 h."

ADME, Psicose, Oral and Parenteral – In a number of places in this section when describing reference 34, it suggests that "[^{14}C]Psicose levels" were determined. It is more likely that radioactivity from the administered [^{14}C]Psicose was measured. This is especially true of the autoradiography study following iv exposure.

Summary - The subchronic section indicates that it was NICNAS rather than the authors of the study that reached the conclusion. Which is correct?

Memorandum

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

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

DATE: September 4, 2020

SUBJECT: Draft Final Report: Safety Assessment of *Scutellaria baicalensis*-Derived Ingredients as Used in Cosmetics (draft prepared for the September 14-15, 2020 meeting of the Expert Panel for Cosmetic Ingredient Safety)

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

Definition – This section should also note that there is an ingredient derived from the "whole plant".

ADME, Animal, Oral - Rather than just saying "(a flavone component of the extract)" and "(another flavone component)", it would be more helpful to the reader if it said "(a glucuronidated flavone)" and "(the aglycone)".

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: September 9, 2020

SUBJECT: Draft Amended Report: Safety Assessment of Silicates as Used in Cosmetics (draft prepared for the September 14-15, 2020 meeting of the Expert Panel for Cosmetic Ingredient Safety)

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

Key Issues

This report should state that that Pyrophyllite is an approved color for cosmetics in the United States. See 21CFR73.2400 that states: "Pyrophyllite may be safely used for coloring externally applied cosmetics, in amounts consistent with good manufacturing practice. " This means that it is not permitted in eye area products or products used on mucus membranes. The identity and specifications for Pyrophyllite included in 21CFR73.1400 should also be added to this report.

Chemical Properties – This section should also note that Sodium Metasilicate is freely soluble in water (based on USP criteria). The water solubility listed in Table 2 for Sodium Metasilicate is 210 g/L.

Additional Considerations

Chemistry, Definition – This section states: “The Panel considered the method of manufacture of these ingredients (whether synthetic or mined) to be of significant importance to safety.” It would be helpful to state why the method of manufacture is important to safety of these ingredients.

Composition/Impurities – In this section, it would be helpful to mention the percent crystallinity information that is presented in Table 3.

Cosmetic Use – The material actually listed in EU Annex IV (colorants) is: "Natural hydrated aluminum silicate, Al2O3.2SiO2.2H2O, containing calcium, magnesium or iron carbonates,

ferric hydroxide, quartz-sand, mica, etc. as impurities". The CIR report should also state that when used as a color in Europe this ingredient must be labeled as CI 77004.

Non-Cosmetic Use, old report summary – It should be made clear that Pyrophyllite is also an approved drug colorant.

Summary - Since the method of manufacture was a concern of the Expert Panel for Cosmetic Ingredient Safety, perhaps some information about how these ingredients are made and why the Expert Panel is concerned should be mentioned in the Summary.

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: September 4, 2020

SUBJECT: Draft Tentative Report: Safety Assessment of Beta-Alanine Diacetic Acid and Tetrasodium Glutamate Diacetate as Used in Cosmetics (draft prepared for the September 14-15, 2020 meeting of the Expert Panel for Cosmetic Ingredient Safety)

The Personal Care Products Council respectfully submits the following comments on the draft tentative report, Safety Assessment of Beta-Alanine Diacetic Acid and Tetrasodium Glutamate Diacetate as Used in Cosmetics.

Key Issue

In addition to the statement provided by Nouryon Chemicals, LLC, the technical name in the Dictionary, L-Glutamic acid, N,N-Bis(Carboxymethyl)-, Tetrasodium Salt, and the CAS No. 51981-21-6 indicates it is the L-isomer. The ECHA dossier is also on the L-isomer. In the Chemical Properties section, it is not correct to state "it is unknown if the ingredient is supplied as the D-, L-, or DL- form". The racemization information was provided to indicate that the L-form does not easily racemize.

Additional Considerations

Introduction - The introduction should indicate that much of the information included in the CIR report is from summaries of studies from an ECHA dossier on the L-isomer.

Definition and Structures – As only the L-isomer is stated as a technical name in the Dictionary, and the CAS number given in the Dictionary is only associated with the L-isomer, it is not necessary to also include the structure of the D-isomer.

Method of Manufacture – The racemization statement does not belong in in the Method of Manufacture section. The statement from Nouryon Chemicals, LLC said that racemization at ambient temperature "takes a very, very long time (many months)", which is not the same as "several months" as stated in the CIR report.

Summary - The Summary should indicate that the safety data from the ECHA dossier is on the L-isomer.

Personal Care Products Council
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Memorandum

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

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

DATE: August 28, 2020

SUBJECT: Tetrasodium Glutamate Diacetate

Nouryon Chemicals, Inc. 2020. Clarification - Tetrasodium Glutamate Diacetate.

August 2020

Clarification – Tetrasodium Glutamate Diacetate

Nouryon Chemicals, LLC indicates that their Tetrasodium Glutamate Diacetate material is in the “L” form.

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: September 4, 2020

SUBJECT: Draft Report: Safety Assessment of Ubiquinone Ingredients as Used in Cosmetics (draft prepared for the September 14-15, 2020 meeting of the Expert Panel for Cosmetic Ingredient Safety)

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

Method of Manufacture – The statement that no methods of manufacture were submitted by industry is not correct as a method of manufacture for Ubiquinone was provided by a cosmetic ingredient supplier.

ADME, Human, Oral, Ubiquinol – The subjects in reference 42 were given oral doses of Ubiquinol. Rather than stating "after 6 h of administration", it should state "6 h after administration" – as it is unlikely that the subjects were administered Ubiquinol orally for 6 hours.

Depigmentation, Ubiquinone – The "S" in PBS stands for "saline" rather than "solution" as stated in this section.

Summary – If the Expert Panel for Cosmetic Ingredient Safety agrees that the risk assessment from the Norwegian Food Safety Authority does not belong in this report, the following paragraph needs to be deleted from the Summary: "The Norwegian Food Safety Authority calculated MoS values for the use of 1% Ubiquinone in a body lotion (10.2), face cream (52.1), hand cream (38.5), and for the overall exposure from cosmetics (8.5). Based upon the $NOAEL_{hypotension}$ and the estimated overall SED for Ubiquinone in cosmetics, the Norwegian Food Safety Authority stated that the overall MoS of 8.5 was sufficient to support the recommended use concentration of 1% Ubiquinone. Based on dermal irritation and sensitization data, Hydroxydecyl Ubiquinone was concluded to be safely used at 0.5% in cosmetic formulations."