Data Supplement

Acrylamide Acrylate Copolymers
Clays
Diatomaceous Earth
Glucosamine
Glycolactones
Hydroxyacetophenone
Portulaca oleracea
Rosa centifolia
Rosa damascena
Starch Phosphates
Ubiquinone
Zeolites

EXPERT PANEL MEETING
MARCH 7-8, 2022

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 3, 2022

SUBJECT: Draft Final Report: Safety Assessment of Acrylamide/Acrylate Copolymers as Used in Cosmetics (March 7-8, 2022, meeting draft)

The Personal Care Products Council respectfully submits the following comments on the draft final report, Safety Assessment of Acrylamide/Acrylate Copolymers as Used in Cosmetics.

Cosmetic Use – The EU entry is for Polyacrylamides, not just Polyacrylamide. Please add the "s".

Summary – Please identify the "substances" listed in the EU cosmetic regulations to which some of the ingredients in this report are linked.

Summary – For the food uses, please revise "are used" to "are permitted for use"

Table 8 – As irritation was not observed, please revise this statement in the Procedure column: "irritation of cornea, iris, and conjunctiva observed on days 1, 2, and 3 post-instillation". It should indicate that that the cornea, iris, and conjunctiva were examined. It should not suggest that irritation was observed as the study concluded that Acrylates/Octylacrylamide Copolymer was not irritating.

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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 3, 2022

SUBJECT: Draft Amended Report: Safety Assessment of Clays as Used in Cosmetics (March 7-8, 2022 meeting draft)

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

Key Issue
Non-Cosmetic Use; Summary – 21 CFR 310.545 lists materials for which "there are inadequate data to establish general recognition of the safety and effectiveness of these ingredients for the specified uses". Therefore, Attapulgite and Hectorite are not approved OTC drugs. Kaolin is a skin protectant and an antidiarrheal active ingredient, but it is not approved as a digestive aid. This needs to be corrected in the Non-Cosmetic Use section and the Summary.

Additional Considerations
Cosmetic Use – In the following, please change the first “in” to “is”: “Kaolin in used in several types of eye makeup preparations”. Please delete “in” in the following: “reportedly used in at up to 2.6% in face powders”.

Cosmetic Use – When describing the EU Color regulations, it should be made clear that the listing is for CI 77004 with the “chemical name” of “Natural hydrated aluminum silicate, Al2O3.2SiO2.2H2O, containing calcium, magnesium or iron carbonates, ferric hydroxide, quartz-sand, mica, etc. as impurities”

Chronic – Please revise the following sentence as it includes “were observed twice”. “Non-dose-dependent significant changes were observed in mean corpuscular hemoglobin, serum calcium, serum vitamin A, and serum iron were observed.”

Genotoxicity; Summary – In the Genotoxicity section, the study on Montmorillonite is under the Hectorite subheading. If available, please indicate how the Montmorillonite was modified.

Depending on the modification, the studies on the modified Montmorillonite may not be relevant to this report.

Carcinogenicity, Parenteral, Attapulgite – Please revise the following: “No concentrations were not reported” (delete “not” or “No”)

Other Parenteral Studies, Bentonite – As it already states that the control paws were injected with Kaolin, it is not clear that the following sentence is needed. “The injection was of Kaolin. “

Case Reports, Montmorillonite – Please revise the following as it appears something is missing: “taken a few weeks indicated”

Occupational Exposure, Attapulgite – Please revise the following sentence as it includes “was observed” twice. “A significant deficit of mortality from nonmalignant respiratory disease was observed based on age, calendar year, and rates was observed.”

Reference 40 and 43 – These references state: “Last Updated 12/28/1999” and “Last Updated 2019.” This is not correct, as Proposition 65 list the NIOSH Pocket Guide have been updated many times since the dates listed.

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

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

DATE: March 3, 2022

SUBJECT: Draft Tentative Report: Safety Assessment of Diatomaceous Earth as Used in Cosmetics (March 7-8, 2022 meeting draft)

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

Short-Term, Subchronic and Chronic – In the text, please either state it was a guideline study, or give some indication of the endpoints that were examined. When adverse effects are observed at all concentrations tested, please also state the lowest dose/concentration tested.

Summary – Please state the hours of exposure for the acute inhalation study.

Discussion – Because Diatomaceous Earth is mined, it does not seem appropriate to state: "continue to use current good manufacturing practices (cGMPs) to limit impurities". Perhaps the Discussion should suggest routine monitoring of heavy metals and crystalline silica (and materials) that may be of concern to the Expert Panel.

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

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

DATE: March 3, 2022

SUBJECT: Draft Tentative Report: Safety Assessment of Glucosamine Ingredients as Used in Cosmetics (March 7-8, 2022 meeting draft)

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

Dermal Penetration – Please indicate the radioactive label and what was labeled. The last sentence stated that "The test substances were found to readily penetrate…" Does this mean they also studied the penetration of niacinamide?

Developmental and Reproductive Toxicity, Oral, Glucosamine – As the study from reference 38 was a dietary study, please clarify if 20 mg/kg is per kg diet, or if this is a dose (mg/kg body weight).

Dermal Irritation and Sensitization – Please state the number of subjects used in the HRIPT of the foundation containing 2% Acetyl Glucosamine.

Discussion – The new HRIPT studies should be mentioned in the Discussion.

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

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

DATE: March 3, 2022

SUBJECT: Draft Tentative Report: Safety Assessment of Glycolactones as Used in Cosmetics (March 7-8, 2022 meeting draft)

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

Introduction – Rather than saying that antiacne agent is not a cosmetic function in the United States, it would be better to state that antiacne agent is considered a drug function in the United States.

Definition and Structure – A heading needs to be added to the Figure. It would be helpful to state how Gluconolactone is involved in glucose-6-phosphate dehydrogenase deficiency.

ADME, Human, Oral – It is not clear what is meant by "No pathological urine constituents were noted." As this is in the ADME section, were they just looking for metabolites of Gluconolactone, or were they also looking at biomarkers of urinary tract toxicity?

Chronic; Summary – The study with meat should be summarized in the Chronic section and the Summary the same way as in the Carcinogenicity section (without mention of the nitrite exposure groups).

Developmental and Reproductive Toxicity – As the exposures in all the studies in this section were during gestation, please call them "developmental toxicity" studies, rather than "reproductive toxicity" studies.

Summary – Please delete "usually" as Gluconolactone used in food must comply with the *Food Chemical Codex* specifications.

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

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

DATE: March 3, 2022

SUBJECT: Draft Report: Safety Assessment of Hydroxyacetophenone as Used in Cosmetics (March 7-8, 2022 meeting draft)

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

Method of Manufacture – It is not clear why it gives a method of manufacture for "a sample of Hydroxyacetophenone". The method of manufacture is for Hydroxyacetophenone from a supplier that sells to the cosmetics industry, not just "a sample".

Short-Term – As body weight gain is normal over the period of a 28-day study, perhaps "body weight gain" should be revised to "changes in body weight gain".

Genotoxicity – Please state the route of exposure for the *in vivo* micronucleus assay in mice.

Ocular Irritation – Please delete the first "maximum" in the following: "A maximum Draize score of 63, out of a maximum score of 110".

Case Reports – It states that the concentration of Hydroxyacetophenone in the face cream was not stated, which implies that the concentration in the eye drops was stated. What was the concentration of Hydroxyacetophenone in the eye drops?

Summary – For a single ingredient report, it does not make sense to state that "Hydroxyacetophenone has the highest number of reported uses" or that "Hydroxyacetophenone has the highest reported maximum concentration of use." It should state the number of uses for Hydroxyacetophenone, and the product categories with the highest number of uses and the highest concentration of use.

Summary – Please state the OECD guideline (422) used for the reproductive and developmental toxicity study in the Summary.

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

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

DATE: March 3, 2022

SUBJECT: Draft Tentative Report: Safety Assessment of *Portulaca oleracea*-Derived Ingredients as Used in Cosmetics (March 7-8, 2022 meeting draft)

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

Key Issue

The following paper by Kumar et al. (2021) Frontiers | Improvement of a Traditional Orphan Food Crop, Portulaca oleracea L. (Purslane) Using Genomics for Sustainable Food Security and Climate-Resilient Agriculture | Sustainable Food Systems (frontiersin.org) needs to be added to the CIR report. This paper includes a table (Table 1) that outlines the use of purslane (*Portulaca oleracea*) in 18 countries. For example, in Sri Lanka, the entire plant is cooked and eaten as a vegetable. In Australia, roots are eaten after roasting and the seed flour is used in cakes.

Additional Considerations

Cytotoxicity – Units of mg/ml should be called concentrations rather than dose.

Sensitization – The dermal LD_{50} should be presented in the Acute Toxicity section.

Summary – Please revise: "significant variability in enzyme and hematological parameters such as urea, creatine, glutathione, and bilirubin" as the none of the examples are enzymes or hematological parameters. Either "enzymes and hematological parameters" needs to be changed, or the examples listed should be enzymes or hematological endpoints.

Discussion – The 2021 Kumar paper suggested above indicates that the whole plant, including the roots is eaten in some countries.

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

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

DATE: March 3, 2022

SUBJECT: Draft Report: Safety Assessment of *Rosa centifolia*-Derived Ingredients as Used in Cosmetics (March 7-8, 2022 meeting draft)

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

Key Issues

Although the composition may be similar, concretes and absolutes should not be presented under the essential oil heading, they should be under the appropriate extract heading. Please read the Dictionary definition for essential oils and waters as it states: "In addition to Essential Oils and Waters there are a number of other types of plant derived preparations. They include, e.g., extracts, juices, gels, saps, tars, gums and powders to name a few. Extracts may include such preparations as tinctures, concretes, resinoids, or absolutes. Extracts are the largest group of plant derived ingredients. Information on the preparation and the approach to providing INCI names for extracts may be found in the Introduction of the Dictionary and Handbook, Part A, "Regulatory and Ingredient Use Information, C. Labeling Reminders, (4) Extracts." The Nomenclature Convention 29 in the Introduction of the Dictionary and Handbook also provides the approach to providing the INCI name for Extracts."

As absolutes and concretes are not terms used in INCI names, it would be helpful if these terms were defined somewhere in this report.

Additional Considerations

Method of Manufacture, Rosa Centifolia Extract – Reference 18 (ChemBook) as given in the reference section does not give details of the method of manufacture. It should be made clear that plant extracts, as included in the Dictionary, do not have to be made with "volatile solvents". What is described is how an absolute is generally made. It would be helpful to state that this is defined as a whole plant extract.

Method of Manufacture, Rosa Centifolia Flower Wax – It would be helpful to note that this type of ingredient is sometimes called a concrete.

Cosmetic Use; Summary - Please state the FDA product categories for which the highest use concentration was reported.

Non-Cosmetic Use – Please indicate what the "4.25 tons per year" represents, the tons of flowers processed, or the tons of essential oil produced?

Dermal Irritation and Sensitization Studies – Please include the number of subjects and the concentrations tested in the human sensitization studies. For the studies provided by RIFM, because the studies say that the materials were tested, it is likely that the materials were tested without dilution. Please confirm this with RIFM.

Photosensitization/Phototoxicity; References – Reference 9 and 10 in the reference section are the same, and only one mouse phototoxicity study from RIFM is included at the end of the report. Therefore, it appears that the same study is summarized twice in this section. The second summary is more accurate as the study indicates that potential phototoxicity was only observed at irritating concentrations, and that occlusion contributed to the effects observed.

Summary – In the Summary, it would be helpful to identify the compound responsible for the anti-mutagenicity activity.

References 19-22 - If SAApedia is going to be used in CIR reports, perhaps the Chinese company behind it (Jinan Changji Co., Ltd.) should be indicated in the references.

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

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

DATE: March 3, 2022

SUBJECT: Draft Final Report: Safety Assessment of *Rosa damascena*-Derived Ingredients as Used in Cosmetics (March 7-8, 2022 meeting draft)

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

Composition/Impurities, Rosa Damascena Flower Oil – The information about the absolute should be presented under the flower extract. It should be made clear that IFRA provided the typical concentrations of components found in *Rosa damascena* absolute.

Composition/Impurities, Flower Wax – It should be made clear that IFRA provided the typical concentrations of components found in *Rosa damascene* concrete.

Cosmetic Use; Summary – As the material sold to the consumer as an essential oil is not added to "finished products" please revise "finished products" to "when applied".

Cosmetic Use – The EU limits for methyl eugenol in other products (such as 0.01% in fine fragrances) should also be included in the Cosmetic Use section.

Short-Term and Subchronic; Summary – It is not clear what was done with the "tissue". Please correct "hydroponic degeneration of the liver". "Hydroponic" has to do with growing plants without soil and is not a histopathology term.

Genotoxicity, In Vitro, Rosa Damascena Flower Oil; Summary – Units of µg/ml should be called concentrations rather than doses.

Dermatological Patch Test Studies – Please correct "close patch" to "closed patch"

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Executive Director - Cosmetic Ingredient Review

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

DATE: March 3, 2022

SUBJECT: Draft Report: Safety Assessment of Starch Phosphates as Used in Cosmetics (March 7-8, 2022 meeting draft)

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

Impurities – Are there additional impurities specifications in JECFA that are not included in the CIR report? This is suggested by the language, "some of the specifications" and "specification for impurities in…. include". All the JECFA impurities specifications should be included in the CIR report and/or the language should be revised to make it clear that all of the specifications are already in the CIR report.

Short-Term, Subchronic and Chronic, Distarch Phosphate Acetate – Which organs were examined in the 14-week study in pigs. What is the reference for this study? The hamster study is cited to reference 8, but it is not clear if the pig study was also found in reference 8.

Developmental and Reproductive Toxicity – Which organs were examined in the multi-generation studies on Distarch Phosphate and Distarch Phosphate Acetate. If these were guideline studies, the guideline used should be stated.

Dermal Irritation and Sensitization; Summary; Table 7 – The Dermal Irritation and Sensitization section describes only one irritation study of a conditioner. The Summary suggests that two conditioners containing 2% Hydroxypropyl Starch Phosphate were studied. Table 7 indicates that there were two conditioners, but only one contained 2% Hydroxypropyl Starch Phosphate, the second product was a control. Please revise the Summary so it correctly reflects the information in Table 7.

Summary – The paragraph starting with: "The skin irritation potential of 2 conditioners…" either needs to be deleted or revised. This paragraph currently includes more information than was

presented in the Dermal Irritation and Sensitization section. The SIOPT of the conditioner is also briefly mentioned in the next paragraph.

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Executive Director - Cosmetic Ingredient Review

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

DATE: March 3, 2022

SUBJECT: Draft Final Report: Safety Assessment of Ubiquinone Ingredients as Used in Cosmetics (March 7-8, 2022 meeting draft)

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

Penetration Enhancement – Reference 39 should be in the dermal penetration section as it examines the effects of two vehicles on the dermal penetration of Ubiquinone. The penetration enhancement section is used for studies of the effect of the ingredient on the penetration of other materials (often drugs).

ADME, Animal, Oral, Hydroxydecyl Ubiquinone – What doses were used in the rat and dog studies?

ADME, Human, Oral, Ubiquinone – What was measured in the serum (reference 40)? Reproductive and Developmental Toxicity; Summary – When describing a developmental toxicity study, please always state the gestation days the dams were treated.

Reproductive and Developmental Toxicity – Please revise the following sentence to make it clear which animals were examined. "Rabbits, dosed at up to 150 mg/kg/d Hydroxydecyl Ubiquinone and observed for teratological abnormalities, displayed chromaturia in the highest dosage group." (Presumably it was the offspring examined for abnormalities and the adults in which chromaturia was observed.)

Miscellaneous Biological Effects, Hydroxydecyl Ubiquinone – Are there any data to support the following statement? "Vitamin K1 is a structurally similar molecule that has the potential to sensitize individuals to Hydroxydecyl Ubiquinone, to cross-react, or cause allergenicity to Hydroxydecyl Ubiquinone."

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Executive Director - Cosmetic Ingredient Review

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

DATE: March 3, 2022

SUBJECT: Draft Tentative Amended Report: Safety Assessment of Zeolites as Used in Cosmetics (March 7-8, 2022 meeting draft)

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

Method of Manufacture – Please revise the following sentence: "The same supplier reports that a synthetic Zeolite subtype as a sodium, potassium and/or calcium salt is produced by combining the above resultant hydrated sodium salt material is added to a water solution of potassium salt (e.g., potassium chloride) and/or calcium salt (e.g., calcium chloride)."

Composition/Impurities – Please correct: "alumosilicates" to "aluminosilicates"

Short-Term, Subchronic and Chronic – Please state the concentration of quartz used as the positive control in the monkey study.

Developmental and Reproductive Toxicity, old report summary – Please state the species used in the long-term ingestion study of clinoptilolite.

Developmental and Reproductive Toxicity – Please state the gestation days of exposure for the developmental studies in mice, hamsters, rats, and rabbits.

Carcinogenicity, Inhalation – In the following: "body weight gains in the treated groups were since to controls", please correct "since" to "similar".

Carcinogenicity, Intrapleural – Please delete the "t" in "weighted"

Dermal Irritation and Sensitization – Please include the number of guinea pigs and persons included in the dermal sensitization studies.

Summary – In the Summary, it would be helpful to state that fibrosis was not observed in the monkeys exposed to the synthetic Zeolite. Please correct: “in an in an EpiSkin® vitro MTT conversion assay”.