Wave 2 Data Supplement

5-Amino-6-Chloro-o-Cresol
BHA
Hyaluronates
MIBK
Octoxynols
Phenyl-Substituted Methicones
Phytosteryl Glutamates
Prostaglandin Analogues
SCCS NoG
Yeast

EXPERT PANEL MEETING
JUNE 12-13, 2023

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: June 1, 2023

SUBJECT: Draft Final Amended Report: Safety Assessment of 5-Amino-6-Chloro-o-Cresol as Used in Cosmetics (draft prepared for the June 2023 meeting)

The Personal Care Products Council respectfully submits the following comments on the draft final amended report, Safety Assessment of 5-Amino-6-Chloro-o-Cresol as Used in Cosmetics.

Chemistry – Rather than just saying that the use of "ortho" in the INCI name is inappropriate, please state an appropriate name, e.g., 2-amino-2-chloro-6-methylphenol.

Cosmetic Use; Summary – As CTFA concentration of use surveys did not start until at least 1998, please delete "survey" in the following: "However, according to industry survey data submitted in 1996,…"

Cosmetic Use – Please note that Europe also has specific labeling requirements for hair dye products.

Dermal Absorption/Penetration – Since only the risk assessment from the 2013 SCCS opinion is included in the CIR report, please delete the following from the description of the dermal penetration study using 2.1%: "The SCCS noted that the mean values + 2 standard deviations were used for calculating the margin of safety."

Genotoxicity – Since only one dose was used in the mouse study, "dose up to 400 mg/kg bw" (which suggests more than one dose was used in the study) should be revised to "dose of 400 mg/kg bw".

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Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Preethi S. Raj, M.Sc., Senior Scientific Analyst/Writer, CIR
Jinqiu Zhu, PhD, DABT, ERT, DCST, CIR Toxicologist
Date: June 2, 2023
Subject: Wave 2 - Response to WVE's comments on BHA

The enclosed comments received from Women's Voices for the Earth (WVE), dated May 25, 2023, on the Re-Review of BHA are submitted for the Panel's review in this Wave 2 submission.

In their comments, WVE suggested that the Panel re-open the safety assessment of Butylated Hydroxyanisole (BHA) based on two pieces of evidence. Firstly, they referred to some concentration of use data obtained from California Safe Cosmetics Program (CSCP) Product Database (https://cscpsearch.cdph.ca.gov). Secondly, they presented sentences extracted from the Abstract of a recently published review paper. CIR staff examined the submitted information and provided further discussion for the Panel's consideration:

i). WVE stated that, *as required by law, manufacturers have filed reports in the California Safe Cosmetics Database for 1,656 cosmetic products currently containing BHA. (320 additional products are included in the database in which it is noted that BHA has been removed or the product discontinued.)*. WVE also provided the concentration of use data for some products listed in CSCP Product Database, such as *a hair conditioner at 15% (150 mg/mL), a hair conditioner at 5.2% (52 mg/mL), a bath oil at 4.5% (45 mg/mL), several shower gels at 0.9% (9 mg/mL)*, etc. However, detailed information regarding these data is not available.

The CSCP Product Database allows for search of personal care products reported by cosmetics companies, but the search is based on product name, brand, company, category or universal product code (UPC). The search cannot be performed based on ingredient (e.g., INCI name or CAS number). CIR staff conducted a search using category term "hair conditioner" and identified two products containing BHA at concentrations of 150 mg/mL and 52 mg/mL, respectively (Table 1). However, these two products have been discontinued as of 10/25/2022, indicating that they are no longer available in the current market. The reason for their discontinuation is unclear, and it raises questions about whether the company producing these products has updated such changes in the FDA VCRP system. Similarly, it is showing that BHA has been removed from the ingredient list of several shower gel products (used at 9 mg/mL) between 2010-2012 (Product ID 48621-48624 in the CSCP database), meaning that these products are no longer formulated with BHA. According to 2023 FDA VCRP data, BHA has 70 reported uses, with the maximum reported concentration of use for BHA in 2023 being 0.15% in other manicuring preparations. Additionally, it is unclear how the WVE derived a 15% use concentration from 150 mg/mL, as the density values of these hair conditioner products are not available in the database.

Table 1. Information of two hair conditioner products included in CSCP Product Database

Product ID	Company	Brand	Product Name	Product Discontinued Date	Product Submitted Date	Ingredient Name	Unit of Measure	Concentration	Ingredient Submitted Date	Product Category
48618	Davines S.p.A.	Davines	NATURAL TECH - AWAKENING - aromatic oil blend	10/25/2022	10/14/2009	Butylated hydroxyanisole (BHA) 25013-16-5	mg/mL	52	10/14/2009	Hair Conditioners (rinse-out)
48619	Davines S.p.A.	Davines	NATURAL TECH - RELAXING - aromatic oil blend	10/25/2022	10/14/2009	Butylated hydroxyanisole (BHA) 25013-16-5	mg/mL	150	10/14/2009	Hair Conditioners (rinse-out)

ii). WVE referenced the following sentences from the Abstract of a review paper (Zhang et al. 2023), and proposed its inclusion in the safety assessment report.

> "*Several studies have shown that BHA could cause thyroid system damage, metabolic and growth disorders, neurotoxicity, and carcinogenesis. Mechanisms such as endocrine disruption, genotoxicity, disturbances of energy metabolism, reactive oxygen species (ROS) production, signaling pathways, and imbalances in calcium homeostasis appear to be associated with the toxic effects of BHA.* ***Avoiding the toxic effects of BHA to the maximum extent possible is a top priority****. Finding safe, non-toxic and environmentally friendly alternatives to BHA should be the focus of subsequent research."*

Zhang et al 2023 is a newly published paper (online May 1, 2023). CIR staff has obtained the full text and extracted the key points of the review for the Panel's consideration, as outlined below:

- *Studies have suggested that BHA is mainly detected in various foods, including fats, oils and their products; cereals and cereal products; vegetables and vegetable products; milk and milk products; meat and meat products; fish, fish products and seafood, etc. In the available studies, the highest concentrations of BHA in edible oil samples were 190 mg/kg. In another study testing the BHA content of commercial cooking oils (soybean oil, olive oil, vegetable oil and oil blends) and fish oil samples, BHA was found to be present in 8 out of 17 samples; the highest level was 135.4 mg/kg, and the lowest level was 14.1 mg/kg.*
- *BHA can also be detected in many environmental media. BHA was found at the highest levels in house dust. 3-BHA (3-tertbutyl-4-hydroxyanisole) was found in house dust in five Chinese cities; the highest concentration was 7.44 mg/kg (range 0.01 - 7.44 mg/kg).*
- In a Canadian study (Liu et al. 2019) on personal care products (n = 214), 3-BHA can be found in 4.2% of samples; the concentration was 0.00393 mg/kg (geometric mean), with a median concentration less than the minimum quantifiable limit (MQL). The maximum detected concentration in personal care products is 1.3 mg/kg.
- *According to documentation from the European Food Safety Authority (EFSA), when BHA is used as a food additive, it is generally considered safe if BHA intake does not exceed the maximum acceptable daily intake (ADI) of 0.5 mg/kg body weight (bw) per day.* This translates to a daily intake of 30,000 µg, assuming a default human body weight of 60 kg.
- In comparison, California's Office of Environmental Health Hazard Assessment (OEHHA) has established a no significant risk level (NSRL) at 4000 µg/day (NSRL is defined as the daily intake level posing a 10^{-5} lifetime risk of cancer).

Considering the exposure data outlined in the review paper by Zhang et al. (2023), it indicates that human exposure to BHA during cosmetic use is minimal. The Panel is anticipated to take into account this supplementary information, along with the new toxicological data presented in the Re-Review document, to decide whether the safety assessment of BHA should be re-opened.

References:

Zhang XJ, Diao MN, Zhang YF. A review of the occurrence, metabolites and health risks of butylated hydroxyanisole (BHA). J Sci Food Agric. 2023 May 1. doi: 10.1002/jsfa.12676.

Liu R, Mabury SA. Synthetic Phenolic Antioxidants in Personal Care Products in Toronto, Canada: Occurrence, Human Exposure, and Discharge via Greywater. *Environ Sci Technol.* 2019;53(22):13440-13448.

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WOMEN'S VOICES FOR THE EARTH

May 25, 2023

Re: Comments on the Re-Review of the Safety Assessment of BHA as Used in Cosmetics

To the CIR Expert Panel,

I am writing both to encourage you to re-open your safety assessment of BHA as used in cosmetics, and to provide you with additional information for your consideration.

1) In the draft, it notes that VCRP data includes just 70 uses of BHA at a maximum concentration of 0.15%. This appears to be underestimating the true use of BHA in cosmetics. BHA is one of the chemicals that is required to be reported to the California Safe Cosmetics Database because BHA is on the California Proposition 65 list as a carcinogen. https://oehha.ca.gov/chemicals/butylated-hydroxyanisole

As required by law, manufacturers have filed reports in the California Safe Cosmetics Database for **1,656** cosmetic products currently containing BHA. (320 additional products are included in the database in which it is noted that BHA has been removed or the product discontinued.)

Not all product reports in the database include the concentration of use, but of those that do, there are a number of products with concentrations greater than 0.15% including:

- a hair conditioner at 15% (150 mg/mL),
- a hair conditioner at 5.2% (52 mg/mL),
- a bath oil at 4.5% (45 mg/mL),
- several shower gels at .9% (9mg/mL)
- a mascara at .5% (5 mg/g)
- several skin creams at .2% (2 mg/mL)
- two nail liquids at .16% (1.6 mg/g)

The database is easily searched here: https://cscpsearch.cdph.ca.gov/search/publicsearch. I am happy to share the products containing BHA data as an Excel file if that is helpful.

In addition, I recommend adding to the safety assessment, a newly published review of health risks of BHA, published in May 2023, which concludes:

> "*Several studies have shown that BHA could cause thyroid system damage, metabolic and growth disorders, neurotoxicity, and carcinogenesis. Mechanisms such as endocrine disruption, genotoxicity, disturbances of energy metabolism, reactive oxygen species (ROS) production, signaling pathways, and imbalances in calcium homeostasis appear to be associated with the toxic effects of BHA.* ***Avoiding the toxic effects of BHA to the maximum extent possible is a top***

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***priority**. Finding safe, non-toxic and environmentally friendly alternatives to BHA should be the focus of subsequent research."*

Citation:

Zhang XJ, Diao MN, Zhang YF. A review of the occurrence, metabolites and health risks of butylated hydroxyanisole (BHA). J Sci Food Agric. 2023 May 1. doi: 10.1002/jsfa.12676.

Thank you for your consideration of these comments.

Alexandra Scranton

Director of Science and Research

Women's Voices for the Earth

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: June 1, 2023

SUBJECT: Final Report: Safety Assessment of Hyaluronates as Used in Cosmetics (draft prepared for the June 2023 meeting)

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

Key Issues

Abstract; Discussion – To be consistent with boilerplate language for impurities, rather than saying that "the ingredients must free of….", it should state that "the cosmetics industry should continue to use the necessary procedures to limit infectious agents, and/or biologically-derived impurities (e.g., nucleic acids, proteins, endotoxins)."

Please delete the following sentence: "Suppliers and users of these ingredients must accept responsibility for assessing that these ingredients are risk-free." Nothing is "risk-free". Cosmetic product manufacturers are responsible for the safety of the products under the intended conditions of use. The products do not need to be "risk-free".

Additional Considerations

Genotoxicity – Please state the route of exposure (oral gavage) used in the mouse micronucleus assays.

Immediate and Delayed Hypersensitivity – The Summary says that 6 fillers were tested. The section where the information is first presented should have more details (or at least the same details) as the Summary. In this section it should also state that 6 fillers were tested.

Cosmetic Ingredient Review

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Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Regina Tucker, M.S. Scientific Analyst/Writer, CIR
Jinqiu Zhu, PhD, DABT, ERT, DCST, CIR Toxicologist
Date: June 2, 2023
Subject: Wave 2 - Response to WVE's comments on MIBK

The enclosed comments received from Women's Voices for the Earth (WVE), dated May 25, 2023, on the Draft Amended Report of MIBK are submitted for the Panel's review in this Wave 2 submission.

In their comments, WVE provided information about several artificial nail activator products containing MIBK, and they suggested the Draft Amended Report should explicitly mention the common presence of MIBK in nail activator products. In the current version, the cosmetic use of MIBK has been categorized under manicuring preparations and shaving preparations (as shown in Table 1 of the Draft Amended Report). According to the 2023 FDA VCRP data, there is one reported use for each category, i.e., one use in other manicuring preparations and one use as aftershave lotion. In the original (2004) report, MIBK was reported to be used in 2 nail polish and enamel remover formulations, and according to an unpublished data submission, it was used at a concentration of 21%, specifically in a nail correction pen (volume = 3 ml).

Nail activator products are a specific type of product used for nail extensions and manicure enhancements. They encompass a range of liquids or sprays that are employed during the nail extension and manicure procedure. Nonetheless, in the FDA VCRP system, nail activator products do not have a designated category code and are likely to be classified under "Other Manicuring Preparations" (Category Code 08G).

The Panel is anticipated to deliberate on the necessity of specifying the application of MIBK in nail activator products.

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WOMEN'S VOICES FOR THE EARTH

May 25, 2023

Re: Comments on the draft Amended Safety Assessment of MIBK as Used in Cosmetics

To the CIR:

I am writing to provide you with additional information to be included in the draft Amended Safety Assessment of MIBK as Used in Cosmetics.

The draft states that VCRP data include just two products containing MIBK, one being a manicuring preparation, and the other being an aftershave lotion.

Our research into nail products has additionally found this ingredient commonly in artificial nail activator products, a product category not well represented in the VCRP data.

Specifically, two manufacturers have reported MIBK in their nail activator products to the California Safe Cosmetics Database.

https://cscpsearch.cdph.ca.gov/search/detailresult/1009

Kiara Sky Dip Essential Seal Protect

Young Nails Slickpour Dip Powder System Activator 3

Our internet research identified an additional six artificial nail activator products also including MIBK as an ingredient:

OPI Powder Perfection Step 2 Activator
https://www.opi.com/products/powder-perfection-step-2-activator
INGREDIENTS: Ethyl Acetate, Methyl Propyl Ketone, **MIBK**, Dimethyltolylamine.

ANC Activator
https://www.amazon.com/Dipping-Powder-System-Liquid-Activator/dp/B019VJKLKY
Ethyl Acetate, Methyl Propyl Ketone, **MIBK** and Dimethyltolylamine.

West Coast Dips Activator
https://westcoastdips.ca/products/dip-activator-refill
Ethylacetate, Methylpropyl Ketone, **Methyl Isobutyl Ketone**, Dimethyl Toluidine

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Double Dip Nails Activator
https://doubledipstore.com/blogs/nail-tutorials/double-dip-powder-ingredients-product-knowledge
Ethylacetate, Methylpropyl Ketone, **Methyl Isobutyl Ketone**, N-N dimethyl-P-toluidine

Adrada Dip Activator
https://adradadippowder.com/activator-3-extreme-shine/
Ethyl Acetate, Methylpropyl Ketone, **Methyl Isobutyl Ketone**, Dimethyl Toluidine.

Karlash Dip System Activator
https://www.amazon.com/Karlash-Powder-System-Refill-Activator/dp/B079MGDHJZ
Ethyl Acetate, Methyl Propyl Ketone, **Methyl Isobutyl Ketone**, Dimethyltoluidine.

The draft Amended Safety Assessment should include information that this chemical is commonly found in nail activator products.

Thank you for your consideration of these comments.

Alexandra Scranton
Director of Science and Research
Women's Voices for the Earth

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: June 1, 2023

SUBJECT: Draft Amended Report: Safety Assessment of MIBK as Used in Cosmetics (draft prepared for the June 2023 meeting)

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

Non-Cosmetic Use, old report summary – Although the CFR citation for the specifications of MIBK used as a denaturant may have been 27CFT21.161 at the time of the original report, it is now 27CFR21.117. This should be made clear in the CIR report.

ADME, Parenteral, old report summary – What was the dose of MIBK in the guinea pig study? It currently states: "Male guinea pigs were administered a single dose of corn oil (450 mg/kg) intraperitoneally."

Acute, Dermal; Summary – In the rabbit study, the dose is 20 ml/kg (given as a volume/Kg bw rather than weight/kg bw). It should not be said that the dose was not stated.

Acute, Inhalation, old report summary – Please correct "pos-exposure" (add "t"). Please revise: "In two groups of 6 exposed rats to test concentrations…."

Developmental and Reproductive Toxicity – Please state the hours/day the rats and mice were exposed by inhalation to MIBK.

Genotoxicity, old report summary – Units of µg/ml should be called concentration not dose.

Carcinogenicity; Summary – In the text, please state the tumor types upon which the NTP reached its conclusions. In the Carcinogenicity section, it would be helpful to note that the mechanism of kidney tumors in male rats is discussed in the Nephropathy section under Other Relevant Studies.

Clinical Studies – Please correct: “s6ix”.

Summary – Please correct: “by the4 Council”. The abbreviation MIBK is used throughout the report, except “methyl isobutyl ketone” is used in the Summary in the paragraph on the field study in 20 workers. In the last paragraph, either add the OECD method number or delete “In accordance”. Please revise the following as the rabbits were observed not MIBK: “In another study MIBK (0.1 ml) was instilled into the eyes of 4 rabbits and observed.”

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Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Preethi S. Raj, M.Sc., Senior Scientific Writer/Analyst, CIR
Jinqiu Zhu, PhD, DABT, ERT, DCST, CIR Toxicologist
Date: June 2, 2023
Subject: Wave 2 - Response to WVE's comments on Octoxynols

The enclosed comments received from Women's Voices for the Earth (WVE), dated May 31, 2023, on the Re-Review of Octoxynols are submitted for the Panel's review in this Wave 2 submission.

In their comments, WVE presented several vaginally-applied douche products that are formulated with Octoxynol-9. In addition, WVE submitted one paper (Pavlova et al. 2000) which analyzed the effect of 7 commercial douche products against various vaginal microorganisms, including Lactobacilli. Further, WVE pointed out "Given that vaginal douche is often used immediately before or after sexual activity, the increased risk of sexually transmitted disease from Octoxynol-9 exposure is of great concern."

In presenting the findings of the Pavlova et al. (2000) study, WVE stated that "A study published in 2000 tested seven brands of commercial douche to assess the effect on vaginal microorganisms. The brand containing Octoxynol-9 killed all healthy vaginal Lactobacillus strains tested." However, CIR staff has identified such statement is not accurate. As demonstrated in Table 1 of the Pavlova et al. (2000) paper, of 7 douche products tested, three contain Octoxynol-9, i.e., Products **A, F,** and **G**. *The results showed that the three products (douches A, D, and E) made of water, **vinegar**, and other ingredients, had no effect (or **mild effect for douche A**) on the growth of vaginal lactobacilli, but selectively inhibited multiple vaginal pathogens. Four products (douches B, C, **F**, and **G**) made of various **antiseptics** showed a significant inhibitory effect against all vaginal microorganisms tested, including vaginal lactobacilli, BV-associated pathogens, group B streptococci, and three Candida species.* The authors further indicated that *In summary, this in vitro study suggested that the antimicrobial effects of the commercial douche products varied among different brands and microbial species tested. The **antiseptic-containing douche** products inhibited all microorganisms tested. The **vinegar-containing** products selectively **inhibited pathogens** associated with vaginal infections, but **not vaginal lactobacilli**.*

Vaginal douches can be considered to *be both drugs (because they are sometimes used to treat disease) and cosmetics (because they cleanse and/or scent part of the body)* (Martino et al, 2002). *Over-the-counter douches differ in composition; the most common active ingredients are **antiseptic compounds** and lactic acid* (van der Veer et al, 2019). Based on this information, Product F and G tested in the Pavlova et al (2000) study may be considered as over-the-counter drugs, and therefore, their safety evaluation falls outside the purview of the Panel. In comparison, Product A (vinegar-containing douche formulated with Octoxynol-9) ***selectively inhibited vaginal pathogens*** *associated with bacterial vaginosis, group B streptococcal vaginitis, and candidiasis, but **not lactobacilli**.*

In another review paper that discussed the risks of vaginal douching to women's health, irrespective of the ingredients formulated in douching products, the authors asserted that "There is a broad consensus that douching should be avoided during pregnancy…again, the preponderance of evidence suggests that douching may be harmful. The authors of the present review believe that there is no reason to recommend that any woman douche and, furthermore, that women should

be discouraged from douching (Martino et al, 2002)." Furthermore, "conflicting results are reported regarding sexually transmitted infections and douching. Some studies suggest that adolescents who douche are more likely to have a history of a sexually transmitted disease, while other studies have found that women who have a history of a sexually transmitted disease were less likely to douche (Martino et al, 2002)."

The Panel is expected to assess the relevance and significance of WVE's submission as part of their decision-making process to determine whether a re-review of Octoxynols is necessary.

Reference:

Pavlova SI, Tao L. In vitro inhibition of commercial douche products against vaginal microflora. *Infect Dis Obstet Gynecol.* 2000;8(2):99-104

Martino JL, Vermund SH. Vaginal douching: evidence for risks or benefits to women's health. *Epidemiol Rev.* 2002;24(2):109-124.

van der Veer C, Bruisten SM, van Houdt R, et al. Effects of an over-the-counter lactic-acid containing intra-vaginal douching product on the vaginal microbiota. *BMC Microbiol.* 2019;19(1):168.

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WOMEN'S VOICES FOR THE EARTH

May 31, 2023

Re: Comments on the Re-Review of the Safety Assessment of Octoxynols

To the CIR:

I am writing to encourage you to re-open the Safety Assessment of Octoxynols to include important information about the potential adverse impacts of Octoxynol-9 from vaginally-applied cosmetics such as douche, on vaginal health and reproductive health.

1) Octoxynol-9 is used in vaginally-applied cosmetics

Although the most recent VCRP data indicates that there are no douches or personal cleansing products reporting the use of Octoxynol-9, our research indicates there are several on the market today. The top-selling brand of douche in the U.S. is Summer's Eve. One version of Summer's Eve douche (Island Splash scent) contains Octoxynol-9. It is worth noting that Octoxynol-9 is the first ingredient (following water). Furthermore, Summer's Eve is a market leader, and numerous generic brands of douche routinely copy Summer's Eve's formulas and even print "Compare to Summer's Eve" on their packaging. We identified two generic brands of douche containing identical ingredients to Summer's Eve douche – both also including Octoxynol-9. As generic brands rarely have an internet presence, it is likely there are even more identical products on the market. (Note – none of the following products are "medicated douches", meaning these products are classified as cosmetics as opposed to drug products by FDA.)

Links to ingredient listings:

Summer's Eve Island Splash Douche
https://www.summerseve.com/feminine-hygiene-products/douche/island-splash
Purified Water, Octoxynol-9, Citric Acid, Sodium Benzoate, Disodium EDTA, Fragrance.

CareOne Fresh Scent Douche
https://1source.com/products/careone-feminine-douche-fresh-scent
Purified Water, Octoxynol-9, Citric Acid, Sodium Benzoate, Disodium EDTA, Fragrance.

New Freshness Tropical Evening Douche
https://www.fooducate.com/product/New-Freshness-Douche-Tropical-Evening/DC6162C6-3D14-11E1-AFF9-1231380C18FB
Purified Water, Octoxynol-9, Citric Acid, Sodium Benzoate, Disodium Edta, Fragrance.

2) Octoxynol-9 containing douche has been shown to significantly inhibit vaginal Lactobacillus, which are bacteria crucial to good vaginal health.

A study published in 2000 tested seven brands of commercial douche to assess the effect on vaginal microorganisms. The brand containing Octoxynol-9 killed all healthy vaginal Lactobacillus strains tested

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in less than a single minute of exposure. (In comparison, the douche brands made with vinegar and water had no effect on Lactobacillus.) A healthy balance of vaginal Lactobacillus is key to vaginal health. Disruption of vaginal microflora (and particularly disruptions leading to low levels of Lactobacillus) is linked to increased risk of bacterial vaginosis, preterm birth, infertility, pelvic inflammatory disease and other conditions. Octoxynol-9 exposure from vaginally applied cosmetics such as douche is of great concern to vaginal health.

Source: Pavlova SI, Tao L. In vitro inhibition of commercial douche products against vaginal microflora. Infect Dis Obstet Gynecol. 2000;8(2):99-104. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1784667/

3) Octoxynol-9 has the capacity to destroy cell membranes and is especially harmful to vaginal epithelial tissue.

Initial studies of nonoxynol-9 used in spermicides resulted in significant damage to vaginal epithelial tissue, resulting in the unfortunate, and unintended consequence of increasing the rate of HIV acquisition, due to the destruction of protective vaginal epithelial tissue. Followup studies of spermicidal sponges and gels containing Octoxynol-9 (Triton X-100) have shown the very same unintended impact. In fact, the studies have shown that Octoxynol-9 severely damages vaginal tissue at exposure levels orders of magnitude below the levels needed for contraceptive effect. Researchers of this study concluded "*Our present results, taken in combination with the results of earlier in vivo studies from other laboratories raise serious doubts as to whether many if not most of the contraceptive sponges and spermicide gels on the market today should be licensed for use at all*." Octoxynol-9 in vaginally applied cosmetics such as douche has the potential to have this same effect. Given that vaginal douche is often used immediately before or after sexual activity, the increased risk of sexually transmitted disease from Octoxynol-9 exposure is of great concern.

Sources:
Inácio ÂS, Mesquita KA, Baptista M, Ramalho-Santos J, Vaz WL, Vieira OV. In vitro surfactant structure-toxicity relationships: implications for surfactant use in sexually transmitted infection prophylaxis and contraception. PLoS One. 2011;6(5):e19850. Available at; https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3095630/

Trifonova RT, Pasicznyk JM, Fichorova RN. Biocompatibility of solid-dosage forms of anti-human immunodeficiency virus type 1 microbicides with the human cervicovaginal mucosa modeled ex vivo. Antimicrob Agents Chemother. 2006 Dec;50(12):4005-10. doi: 10.1128/AAC.00588-06. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1693981/

Cone RA, Hoen T, Wong X, Abusuwwa R, Anderson DJ, Moench TR. Vaginal microbicides: detecting toxicities in vivo that paradoxically increase pathogen transmission. BMC Infect Dis. 2006 Jun 1;6:90. doi: 10.1186/1471-2334-6-90. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1523343/

Thank you for your consideration of these comments.

Alexandra Scranton
Director of Science and Research
Women's Voices for the Earth

Cosmetic Ingredient Review

Commitment & Credibility since 1976

Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Preethi S. Raj, M.Sc., Senior Scientific Writer/Analyst, CIR
Jinqiu Zhu, PhD, DABT, ERT, DCST, CIR Toxicologist
Date: June 2, 2023
Subject: Wave 2 - Response to WVE's comments on Phenyl-Substituted Methicones

The enclosed comments received from Women's Voices for the Earth (WVE), dated May 31, 2023, on the draft tentative report of phenyl-substituted methicones are submitted for the Panel's review in this Wave 2 submission.

In their comments, WVE presented a recently published paper (online Feb 16, 2023),[1] which contains droplet/particle size distribution data of 78 cosmetic sprays using a laser diffraction system for the measurement (determining droplet/particle diameters ranging from 0.1 μm to 900 μm). The study results indicate that the level of respirable droplets/particles remitted by **pump sprays** averaged **0.5%** among all measured particles (n = 63, range 0.00% - 2.23%), while that released by **propellant-based sprays** averaged **15.25%** (n = 15, range 0.15% - 32.27%). **Dry shampoos** in powder form (n = 8) exhibited the highest percentage of respirable droplets/particles, ranging from 16.66% to 32.27%. Based on the analysis, the authors suggested a default value of **25%** of respirable droplets/particles for dry shampoos. Please note the authors have indicated in the discussion that "it is **difficult to interpret the results** obtained on only 15 **propellant-based sprays**, more **confidence is placed in the pump spray** data due to larger sample size. **Additional data is still required for each product type.**" Please also note in the current study, dry shampoos were classified as propellant-based hairsprays (by the authors), while they are not specifically categorized in the FDA VCRP system or discussed in the newly updated SCCS Note of Guidance for the testing of cosmetic ingredients and their safety evaluation (the 12th revision published on May 16, 2023).

Importantly, under the Material and Methods section, the authors stated "Droplet/particle size distribution was assessed using a laser diffraction system according to ISO 13320–2020." But no more details were provided regarding the experimental procedures. It is not clear to what extent such a test mimics the realistic in-use conditions of each specific type of cosmetic sprays. As discussed in another review paper,[2] there are special aspects that need be considered in the safety evaluations of cosmetic sprays, e.g., utilizing reality-based mathematical models, such as ConsExpo 4.1 or BG-Spray, to quantify aerosol concentrations over time.

Nonetheless, these emerging data broaden, to some degree, our knowledge of airborne droplets/particles emitted during the application of pump and propellant-driven sprays. Previous data, as summarized in the CIR Respiratory Exposure Resource Document, indicated that "Typically, **< 1%** of the airborne droplets/particles released from pump sprays are in the range considered to be respirable (i.e., d_{ae} < 10 μm). In comparison, the median d_{ae} of the airborne droplets/particles of propellant hair sprays range from 25 μm to 50 μm.[2-4] Usually, 1% to 2.5%, but no more than 5%, of the droplets/particles emitted from propellant hair sprays are within the respirable range,[3,5] while a larger fraction of respirable particles would be released from propellant deodorant sprays, as reported by simulated test data, in silico model outputs, and industry survey.[4,6-9] The available data, however, are insufficient to determine median particle sizes (and distributions) resulting from airbrush device use. Thus, the fraction of respirable particles that would be released by applying cosmetics with airbrush devices is unknown." (See pdf page 3 of the CIR Respiratory Exposure Resource Document at https://www.cir-safety.org/sites/default/files/report_InhalationDocument_122021.pdf.) In the current study, the authors re-affirmed the finding that "most of the cosmetic **pump sprays** tested released a very low percentage of respirable droplets/particles (**<1%**)", while

propellant-based sprays released a higher percentage of respirable particles compared to data in previous literature. In this regard, the Panel is expected to take into account the findings presented in this study for relevant inhalation risk evaluation.

Meanwhile, it is relevant to point out that a tiered approach for inhalation safety evaluation has been outlined in the CIR Respiratory Exposure Resource Document with emphasis that "It is important to note that the final exposure is determined **not only by the particle size**, but also the distribution of particles/droplets in the exposure room under in-use conditions. The composition of the formulation and the spray characteristics are of significant impact." (See pdf page 9 of the CIR Respiratory Exposure Resource Document.) "The Panel recognizes that the distribution of aerodynamic equivalent diameters of cosmetic aerosol droplets/particles is an important parameter determining where the inhaled particles/droplets will be deposited in the respiratory tract. However, the Panel also emphasizes that **the chemical properties** of the particles/droplets will be critical factors determining whether they will cause inhalation toxicity where they are deposited." (See pdf page 11 of the CIR Respiratory Exposure Resource Document.) Therefore, "the Panel will continue to **review all of the relevant inhalation toxicity, use, and other data** to determine the safety of cosmetic ingredients. The Panel will evaluate the importance of the inhalation route for assessing the safety of an ingredient or group of ingredients, and evaluate data that may be available to estimate potential respiratory doses from aerosolized products." (See pdf page 11 of the CIR Respiratory Exposure Resource Document.)

WVE further submitted several dry shampoo products, along with the general method of application, that are formulated with phenyl-substituted methicones, in particular, Phenyl Trimethicone. While information regarding product formulations is included in WVE's submission, please note that the use concentration of each ingredient is not provided. (Under this scenario, conducting a risk assessment is not feasible.) Further, new data pertaining to Phenyl Trimethicone have been incorporated in the draft tentative report of phenyl-substituted methicones (highlighted in yellow), which cover the endpoints of inhalation, acute dermal toxicity, repeated-dose oral toxicity, oral DART, genotoxicity, ocular irritation, dermal irritation, and sensitization.

The Panel is anticipated to consider the additional information presented above, along with the new data that have been incorporated into the draft tentative report, to issue a conclusion regarding the use of phenyl-substituted methicones in cosmetics.

Reference:

1. Berrada-Gomez MP, Bui B, Bondarenko H, Ferret PJ. Particle size distribution in the evaluation of the inhalation toxicity of cosmetic spray products. *Regul Toxicol Pharmacol.* 2023;139:105359.
2. Rothe H, Fautz R, Gerber E, et al. Special aspects of cosmetic spray safety evaluations: Principles on inhalation risk assessment. *Toxicol Lett.* 2011;205(2):97-104.
3. Rothe H. Special aspects of cosmetic spray safety evaluation. Unpublished information presented at the 26 September 2011 CIR Expert Panel Meeting. Washington, DC. 2011.
4. Delmaar JE, Bremmer HJ. *The ConsExpo Spray Model.* 2009. RIVM 320104005/2009.
5. European Aerosol Federation (FEA). *Guide on Particle Size Measurements from Aerosol Products.* Belgium. 2009.
6. Bremmer HJ, Lodder LCHPhd, Engelen JGMv. *Cosmetics Fact Sheet: To assess the risks for the consumer; Updated version for ConsExpo 4.* 2006. RIVM 320104001/2006.
7. Tuinman IL. *Aerosols from Spray Cans and Trigger Sprays. Particle Size Distributions and Spreading in a Closed Environment.* 2004. TNO report PML 2004-C106.
8. Tuinman IL. *Particle size distributions of aerosols from spray cans and trigger sprays.* 2007. TNO report august 2007.
9. CIR Science and Support Committee of the Personal Care Products Council (CIR SSC). Comments on Draft Revised CIR Precedent - Aerosols Document/Submission of Aerosol Particle Size Data. Unpublished data submitted by the Personal Care Products Council. In:2018.

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WOMEN'S VOICES FOR THE EARTH

May 31, 2023

Re: Comments on the draft Safety Assessment of Phenyl-Substituted Methicones as Used in Cosmetics.

To the CIR:

I am writing to provide you with additional information on inhalation hazards for your assessment of Phenyl-Substituted Methicones.

1) **Newly published study reveals that cosmetic aerosol sprays, (and particularly dry shampoo sprays) emit considerable amounts of particles small enough to be deeply inhaled.**

I would like to bring your attention to a newly published study assessing the particle size distribution from cosmetic spray products. Contrary to the CIR boilerplate, which claims that most particles from a cosmetic spray would not be respirable, this study of 78 cosmetic sprays found that aerosol sprays (but not pump sprays) emitted a considerable number of respirable droplets/particles smaller than 10 microns in diameter. Specifically, propellant (aerosol) sprays averaged 15% of particles emitted were respirable, and of greatest concern were the category of aerosol dry shampoo sprays for which, on average, 25% of particles emitted would be small enough to be deeply inhaled into the lungs. Aerosol dry shampoos (which are spray powder products) appear to be a particularly concerning category of cosmetic product for inhalation, not unlike airbrush cosmetics. Additional consideration of inhalation hazards from aerosol cosmetic sprays, based on this data should be included in CIR safety assessments.

Source: Berrada-Gomez MP, Bui B, Bondarenko H, Ferret PJ. Particle size distribution in the evaluation of the inhalation toxicity of cosmetic spray products. Regul Toxicol Pharmacol. 2023 Mar;139:105359. https://pubmed.ncbi.nlm.nih.gov/36805297/

2) **Dry Shampoo aerosol spray products commonly contain phenyl-subsituted methicones.**

It appears the VCRP data does not specify if a cosmetic spray product is in the dry shampoo category. I searched online for ingredient listings of dry shampoo products – and found many aerosol dry shampoos containing phenyl-substituted methicones. Of particular concern, is that the most common methicone ingredient in dry shampoos is phenyl trimethicone, which has been associated with acute inhalation toxicity.

The inhalation exposure to dry shampoos can also be considerable when directions for use are followed. For example, one brand's package instructions states:

1. Shake well.
2. Section hair and apply product in a sweeping motion to dirty and oily areas.
3. Wait 30 seconds.

PO Box 8743, Missoula, MT 59807 406.543.3747 www.womensvoices.org womensvoices@womensvoices.org

4. Remove excess powder by massaging and shaking at roots with fingers or brush.
5. Shake and repeat if necessary.
6. Apply before bed for oil absorption while you sleep.

Thus, the initial spray application may occur multiple times (as each section of hair is sprayed). Following that, any excess product on the hair is brushed or shaken out, resuspending particles in the immediate breathing zone. Then a suggestion to "repeat if necessary" is given, followed by the suggestion of an additional application of the product before bed.

Dry Shampoo products contain the following Phenyl-substituted Methicones:

- Phenyl Trimethicone
- Diphenylsiloxy phenyl trimethicone
- Polymethylsilsesquioxane
- Trimethylsiloxyamodimethicone,
- Aminopropyl Phenyl Trimethicone
- Trisiloxane

Examples:

Saints & Sinners Superfresh Divine Dry Shampoo

https://www.amazon.com/SUPERFRESH-No-Residue-Cleansing-Nourishing-Volumizer/dp/B09FRH8Z93

Hydrofluorocarbon 152a, SD Alcohol 40-B (Alcohol Denat.), Hydrolyzed Rice Protein, Panthenol, Phenyl Trimethicone, Tocopheryl Acetate**, Silica** , Aluminum Starch Octenylsuccinate, Cyclopentasiloxane, Benzyl Alcohol , Potassium Sorbate , Sodium Benzoate, Fragrance (Parfum) , Hexyl Cinnamal , Limonene, Linalool , Water (Aqua, Eau)

AG Care Simply Dry Shampoo

https://www.cosmoprofbeauty.com/USA-031326.html

AQUA (WATER/EAU), CETEARYL ALCOHOL, BEHENTRIMONIUM CHLORIDE, CAPRYLIC/CAPRIC TRIGLYCERIDE, CETYL ALCOHOL, HYDROXYPROPYL STARCH PHOSPHATE, POLYSORBATE 60, POLYQUATERNIUM-70, QUATERNIUM-91, **AMODIMETHICONE**, CETRIMONIUM CHLORIDE, GLYCERIN, CETRIMONIUM METHOSULFATE, DIPHENYLSILOXY PHENYL TRIMETHICONE, **PERFLUORONONYL DIMETHICONE**, PHENOXYETHANOL, PARFUM (FRAGRANCE), QUATERNIUM-87, BUTYROSPERMUM PARKII (SHEA) BUTTER, GLYCERYL POLYACRYLATE, COCOS NUCIFERA (COCONUT) OIL, DIPROPYLENE GLYCOL, PROPYLENE GLYCOL, ARGANIA SPINOSA KERNEL OIL, PANTHENOL, TRIDECETH-12, CINNAMIDOPROPYLTRIMONIUM CHLORIDE, **DIMETHICONE PEG-8 MEADOWFOAMATE**, TETRASODIUM EDTA, HELIANTHUS ANNUUS (SUNFLOWER) SEED EXTRACT, HYDROLYZED PEA PROTEIN, HYDROLYZED VEGETABLE PROTEIN, BENZYL ALCOHOL, COUMARIN, IODOPROPYNYL BUTYLCARBAMATE, TRIS(TETRAMETHYLHYDROXYPIPERIDINOL) CITRATE, CALENDULA OFFICINALIS FLOWER EXTRACT, DIANTHUS CARYOPHYLLUS FLOWER EXTRACT, LAVANDULA ANGUSTIFOLIA (LAVENDER) EXTRACT, PINUS PALUSTRIS LEAF EXTRACT, TRIFOLIUM PRATENSE (CLOVER) EXTRACT.

L'ANZA Healing Style Dry Shampoo

https://www.lovelyskin.com/o/lanza-healing-style-dry-shampoo

Keratin, Propane, Butane, Isobutane, Alcohol Denat, Aluminum Starch Octenylsuccinate, KERATIN AMINO ACIDS, Hectorite, Undaria Pinnatifida Extract, Mentha Piperita (Peppermint) Leaf Extract, Oryza Sativa (Rice) Bran Extract, Rosmarinus Officinalis (Rosemary) Leaf Extract, HELIANTHUS ANNUUS (SUNFLOWER) EXTRACT, Tocopherol, Cereus Grandiflorus (Cactus) Flower Extract, **DIMETHICONE PEG-8 MEADOWFOAMATE**, Sodium PCA, MAGNESIUM PCA, Zinc PCA, MANGANESE PCA, **SILICA DIMETHICONE SILYLATE**, Cyclopentasiloxane, Phenyl Trimethicone, Water/Eau (AQUA), Sodium Benzoate, Potassium Sorbate, Chlorphenesin, Benzoic Acid, Sorbic Acid, Phenoxyethanol, Fragrance (Parfum), Limonene, Hexyl Cinnamal, Linalool

Davines Hair Refresher (Dry Shampoo Spray)

https://accentofstyle.com/products/hair-refresher

BUTANE, PROPANE, ISOBUTANE, ORYZA SATIVA STARCH / ORYZA SATIVA (RICE) STARCH, CYCLOPENTASILOXANE, ALCOHOL DENAT., PHENYL TRIMETHICONE, CITRONELLYL METHYLCROTONATE, PARFUM / FRAGRANCE, **SILICA** SILYLATE, LIMONENE.

Kevin Murphy Doo.Over Dry Powder spray

https://utiee.com/dry-shampoos-hair-powders/261-dooover-km.html

Hydrofluorocarbon 152a, Alcohol Denat., Butane Octylacrylamide/Acrylates/Butylaminoethyl Methacrylate Copolymer, Tapioca Starch, Pogostemon Cablin Oil, Juniperus Virginiana Oil AMP-Isostearoyl Hydrolyzed Wheat Protein, Phenyl Trimethicone, Magnesium Stearate, **PEG/PPG-17/18 Dimethicone**, Triethyl Citrate, Polymethylsilsesquioxane, Ethylhexyl Methoxycinnamate, Aminomethyl Propanol, BHT, Fragrance (Parfum), Benzyl Benzoate, Hydroxyisohexyl 3-Cyclohexene Carboxaldehyde, Hydroxycitronellal, Benzyl Salicylate, Butylphenyl Methylpropional, Linalool, Isoeugenol

Ouidad Clean Sweep Moisturizing Dry Shampoo

https://incidecoder.com/products/ouidad-clean-sweep-moisturizing-dry-shampoo

Hydrofluorocarbon 152A, Isododecane, Cyclopentasiloxane, Isopropyl Palmitate, Cyclohexasiloxane, Hydrolyzed Ceratonia Siliqua Seed Extract, Citrullus Lanatus (Watermelon) Seed Oil, Dimethicone, Bambusa Vulgaris (Bamboo) Extract, Superoxide Dismutase, Helianthus Annuus (Sunflower) Seed Oil, Vitis Vinifera (Grape) Seed Oil, Olea Europaea (Olive) Fruit Oil, Persea Gratissima (Avocado) Oil, Simmondsia Chinensis (Jojoba) Seed Oil, Passiflora Edulis Seed Oil, Tocopherol, Juglans Regia (Walnut) Seed Oil, Macadamia Ternifolia Seed Oil, Argania Spinosa Kernel Oil, Ethylhexyl Methoxycinnamate, Zea Mays (Corn) Starch, Polyquaternium-7, Schinziophyton Rautanenii Kernel (Mongongo) Oil, Guar Hydroxypropyltrimonium Chloride, Propylene Glycol, Phenyl Trimethicone, Aqua/Water/Eau, Phospholipids, Glycerin, Fragrance (Parfum), Benzyl Salicylate, Citral, Hexyl Cinnamal, Limonene, Linalool

Unwash Color Care Dry Cleanser

https://unwash.com/products/color-care-dry-cleanser

Dimethyl Ether Alcohol Denat. Aluminum Starch Octenylsuccinate Glycerin Propylene Glycol Panthenol Tocopheryl Acetate Volcanic Ash, Actinidia Chinensis (Kiwi) Fruit Extract Aloe Barbadensis Leaf Extract Hedychium Coronarium Root Extract Mangifera Indica (Mango) Fruit Extract Passiflora Incarnata Flower Extract, Aminopropyl Phenyl Trimethicone Helianthus Annuus (Sunflower) Seed Extract PEG/PPG-17/18 Dimethicone AMP-Isostearoyl Hydrolyzed Wheat Protein Ethylhexyl Methoxycinnamate Silica Butylene Glycol Water (Aqua) BHT Benzoic Acid Sorbic Acid Phenoxyethanol Chlorphenesin Lactobacillus Ferment Fragrance (Parfum) Benzyl Alcohol Benzyl Salicylate Hexyl Cinnamal Hydroxyisohexyl 3-Cyclohexene Carboxaldehyde.

Big Sexy Hair Dry Shampoo

https://www.sexyhair.com/product/big-dry-shampoo/

Isobutane, SD Alcohol 40-B (Alcohol Denat.), Propane, Zeolite, PPG-12-Buteth-16, PEG-12 Dimethicone, Helianthus Annuus (Sunflower) Seed Extract, Glycerin, Tetrahexyldecyl Ascorbate, Butylene Glycol, C11-15 Pareth-7, C12-16 Pareth-9, Trimethylsiloxyamodimethicone, Trideceth-12, Polyquaternium-59, Butyl Methoxydibenzoylmethane, BHT, Triclosan, Fragrance (Parfum),Limonene, Lilial, Linalool.

Bumble and bumble. Pret-a-Powder Tres Invisible Dry Shampoo

https://www.ulta.com/p/pret-a-powder-tres-invisible-dry-shampoo-xlsImpprod17771715?sku=2542291

Isobutane, Alcohol Denat., Butane, Dimethylimidazolidinone Rice Starch, Oryza Sativa (Rice) Starch, **Montmorillonite, Illite, Dimethicone, Trisiloxane**, Cetrimonium Chloride, Rhodiola Rosea Root Extract, Amp-Isostearoyl Hydrolyzed Wheat Protein, Argania Spinosa Kernel Oil, Trimethylsiloxyamodimethicone, Diisopropyl Adipate, Panthenol, Polyquaternium-59, Glycerin, Water\Aqua\Eau, C11-15 Pareth-7, C12-16 Pareth-9, Trideceth-12, Silicone Quaternium-16, Undeceth-11, Undeceth-5, Butyloctanol, Butylene Glycol, Pentylene Glycol, Ethylhexyl Methoxycinnamate, Fragrance, Hexyl Cinnamal, Linalool, Citronellol, Limonene, Butylphenyl Methylpropional, Phenoxyethanol.

Tri Aero Dry Shampoo

https://sleekshop.com/products/tri-aero-dry-shampoo.html?sku=tri05-3-0-oz

Isobutane, SD Alcohol 40-B (Alcohol Denat.), Propane, **Zeolite**, PPG-12-Buteth-16, PEG-12 Dimethicone, Helianthus Annuus (Sunflower) Seed Extract, Glycerin, Tetrahexyldecyl Ascorbate, Butylene Glycol, C11-15 Pareth-7, C12-16 Pareth-9, Trimethylsiloxyamodimethicone, Trideceth-12, Polyquaternium-59, Butyl Methoxydibenzoylmethane, BHT, Triclosan, Fragrance (Parfum),Limonene, Lilial, Linalool.

Virtue Refresh Dry Shampoo

https://dermwarehouse.com/product/virtue-refresh-dry-shampoo/

Aqua (Water, Eau), Propylene Glycol, Cyclopentasiloxane, Cetearyl Alcohol, **Caprylyl Methicone,** Keratin, Marrubium Vulgare Extract, Glycerin, Aspartic Acid, PCA, Glycine, Alanine, Serine, Valine, Threonine, Proline, Isoleucine, Phenylalanine, Histidine, Ethylhexylglycerin, Tocopherol, Sodium Lactate, Arginine, Undeceth-5, C12-16 Pareth-9, Undeceth-11, Sodium PCA, Butyloctanol, PEG-12 Dimethicone, Parfum (Fragrance), Behentrimonium Chloride, Potassium Sorbate, PPG-3 Benzyl Ether Myristate, PEG-12 Allyl Ether, Trimethylsiloxyamodimethicone, PEG-12, Silicone Quaternium-16, C11-15 Pareth-7, Benzophenone-4, Trideceth-12, Butylene Glycol, Quaternium 91, Citric Acid, Phenoxyethanol, Linalool, Benzyl Salicylate, Hydroxycitronellal, Limonene, Geraniol, Citronellol, Citral.N79 Tapioca Starch, **Kaolin**

My Hair. My Canvas. Another Day dry shampoo

https://alternahaircare.com/products/my-hair-my-canvas-another-day-natural-dry-shampoo

Isobutane, Alcohol Denat. (SD Alcohol 40-B), Dimethylimidazolidinone Rice Starch, **Zeolite**, Aqua/Water/EAU, C12-15 Alkyl Benzoate, Trisiloxane, Parfum/Fragrance, Cetrimonium Chloride, Trimethylsiloxyamodimethicone, Benzyl Salicylate, C11-15 Pareth-7, Glycerin, C12-16 Pareth-9, Trideceth-12, Linalool, Citronellol, Limonene, Phenoxyethanol, Charcoal Powder, Polysilicone-15, Phospholipids, Caulerpa Lentillifera Extract, Helianthus Annuus (Sunflower) Seed Oil, Sodium Benzoate, Citric Acid.

Moroccanoil Dry Shampoo

https://bluemercury.com/products/moroccanoil-dry-shampoo-light

Aqua/Water/Eau, Sodium C14-16 Olefin Sulfonate, Cocamidopropyl Betaine, Cocamidopropylamine Oxide, Parfum/Fragrance, Guar Hydroxypropyltrimonium Chloride, Argania Spinosa (Argan) Kernel Oil, Peg-40 Hydrogenated Castor Oil, Acrylates Copolymer, Peg-150 Distearate, Glycol Stearate, Hydroxyacetophenone, Algin, Glycerin, Chitosan, Trideceth-9, C12-13 Pareth-9, C11-15 Pareth-7, C12-16 Pareth-9, Silica Dimethyl Silylate, Isopropyl Alcohol, Trideceth-12, Citric Acid, Coconut Acid, Cocamidopropyl Dimethylamine, Caprylyl Glycol, Cetrimonium Chloride, Sodium Glycolate, Ci 60730 (Ext. Violet No. 2), Trimethylsiloxyamodimethicone, Caprylic/Capric Triglyceride, Phenoxyethanol, Chlorphenesin, Potassium Sorbate, Sodium Benzoate, Alpha-Isomethyl Ionone, Linalool. Mopps02

R+Co. Death Valley Dry Shampoo

https://bluemercury.com/products/r-and-co-death-valley-dry-shampoo

Butane, Propane, Sd Alcohol 40-B (Alcohol Denat.), Aluminum Starch Octenylsuccinate, **Silica**, **Cyclomethicone**, Tocopherol, Hydrolyzed Rice Protein, Aminopropyl Phenyl Trimethicone, Panthenol,

Benzophenone-4, Parfum/Fragrance, Alpha-Isomethyl Ionone, Citronellol, Geraniol, Hydroxycitronellal, Limonene.

Thank you for your consideration of these comments.

Alexandra Scranton
Director of Science and Research
Women's Voices for the Earth

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: June 1, 2023

SUBJECT: Draft Final Report: Safety Assessment of Phytosteryl Glutamates as Used in Cosmetics (draft prepared for the June 2023 meeting)

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

Short-Term; Summary – There is not a second 28-day oral study of Phytosteryl/Octyldodecyl Lauroyl Glutamate. It is the same study submitted twice. Reference 13 of the meeting draft summarizes the same study completed at RCC in 1999 (reference 14).

Sensitization – Please state the induction (intradermal, epidermal) and challenge concentrations used in the three guinea pig maximization studies: Phytosteryl/Behenyl/Octyldodecyl Lauroyl Glutamate (25% intradermal, 100% epidermal, 100% challenge); Phytosteryl/Behenyl/Octyldodecyl/Isostearyl Lauroyl Glutamate (10% intradermal, 100% epidermal, 50 and 100% challenge); Phytosteryl/Octyldodecyl Lauroyl Glutamate (5% intradermal, 100% epidermal, 10% challenge).

Tables 4 and 5 – When an OECD method is stated, it is not necessary to state: “No other details provided”. If a reader wants more details, they can look up the stated OECD method.

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: June 1, 2023

SUBJECT: Draft Report: Safety Assessment of Ethyl Tafluprostamide and Isopropyl Cloprostenate as Used in Cosmetics (draft prepared for the June 2023 meeting)

The Personal Care Products Council respectfully submits the following comments on the draft report, Safety Assessment of Ethyl Tafluprostamide and Isopropyl Cloprostenate as Used in Cosmetics.

Key Issues

The submission on Ethyl Tafluprostamide from Dr. John Bailey includes a list of studies planned or underway (p.9 of the submission; pdf p. 180) and indicates that they will be provided to CIR in August/September 2023. It would have been helpful to note this in the memo with the CIR report.

Memo – The memo incorrectly states the use concentration of Ethyl Tafluprostamide as "0.012 to 0.2%". This should be "0.012 – 0.02%" as stated in the Cosmetic Use Section of the report.

Cosmetic Use – The units for the dose of Isopropyl Cloprostenate are wrong. The document (reference 7) says "0.0000084 and 0.000013 mg per use". The CIR report says "8.4 and 13 mg Isopropyl Cloprostenate, per usage". If given as mg, the numbers should be corrected. If the values of 8.4 and 13 are used in the CIR report, the units need to be changed to nanograms (ng not mg).

Submissions from industry provided instructions for use on products containing these ingredients. This information should have been included in the Cosmetic Use section.

Additional Considerations

Dermal Absorption – It should be noted that the amount of Ethyl Tafluprostamide estimated to be absorbed is per use.

Dermal Irritation and Sensitization - The number of HRIPTs completed on products containing Isopropyl Cloprostenate should be stated as well as the number completed under semi-occlusive conditions versus other conditions.

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Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Jinqiu Zhu, PhD, DABT, ERT, DCST, CIR Toxicologist
Date: June 2, 2023
Subject: Wave 2 - Updates in the 12th Revision of the SCCS Notes of Guidance

The following document is provided exclusively for your information; no action is requested herein. On May 16, 2023, the Scientific Committee on Consumer Safety (SCCS) in Europe published the 12th revision of the Notes of Guidance (NoG) for the testing of cosmetic ingredients and their safety evaluation. (This document can be accessed at https://health.ec.europa.eu/system/files/2023-05/sccs_o_273.pdf.)

In the current iteration, the NoG has undergone substantial updates, particularly focusing on incorporating relevant toxicological tools for the safety evaluation of cosmetic ingredients. The importance of systematic literature review has been emphasized, with specific considerations for assessment of quality and risk of bias depending on the toxicological endpoint and type of study, respectively. Notably, there have been significant advancements in animal-free alternative methods or New Approach Methodologies (NAMs); e.g., NAMs for local (acute) toxicity became available and have been validated for regulatory purposes. These changes encompass acute inhalation, skin irritation testing, eye irritation testing with DAL (defined approach for eye irritation, Liquid), and DASS (defined approaches for skin sensitization). Additionally, new in vitro methods for genotoxicity testing, such as 3D skin Comet and in vitro micronucleus, along with advancements of in silico prediction capabilities, have been integrated.

Emphasis has been placed on the significance of Adverse Outcome Pathway (AOP), Integrated Approaches to Testing and Assessment (IATA), as well as Next Generation Risk Assessment (NGRA), as a possible framework for the safety evaluation of cosmetic ingredients, including the definition of concepts such as Bioactivity/Exposure Ratio (BER) and internal Threshold of Toxicological Concern (iTTC). The updates also involve new reporting requirements for carcinogenic, mutagenic, and reprotoxic (CMR) substances and endocrine-active substances. The introduction of non-monotonic dose response for endocrine-active substances and reporting requirements has been discussed. Special attention has been given to the exposure of children to various cosmetic product categories based on their age (e.g., when a cosmetic ingredient is suspected as having potential endocrine activity). Furthermore, templates for the description of the Physiologically Based Toxicokinetics (PBTK) model and parameter verification and analysis have been included. Human Biomonitoring (HBM) in combination with the PBPK model for exposure assessment has been explored.

These revisions serve to reflect the latest scientific understanding and ensure a more comprehensive approach towards safety assessment. The mechanistic rationale and principle underpinning the application of an NGRA to cosmetics may be applied to the safety evaluations carried out by CIR.

Reference:

Scientific Committee on Consumer Safety (SCCS). Notes of guidance for the testing of cosmetic ingredients and their safety evaluation - 12th revision. 2023. SCCS/1647/22. https://health.ec.europa.eu/system/files/2023-05/sccs_o_273.pdf. Accessed 05/30/2023.

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: June 1, 2023

SUBJECT: Revised Draft Report: Safety Assessment of Yeast-Derived Ingredients as Used in Cosmetics (draft prepared for the June 2023 meeting)

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

The February 7, 2022 submission included information on ingredients made from the following species being sold under a "Yeast" name that do not appear in the data profile table: *Candida oleophila, Candida magnoliae, Debaryomyces nepalensis, Metschnikowia pulcherrima*, and *Pichia naganishii.*

In the Memo, it would have been helpful to note why 3 ingredients (Hydrolyzed Yeast Protein, Yeast Beta-Glucan, and Yeast Polysaccharides) were removed from the report.

Method of Manufacture – The following is not complete: "Unpublished data were submitted describing methods of manufacture for some"

Composition and Impurities, *Phaffia rhodozyma* – It would be helpful to state the class of compound in the same order as the compounds are presented, e.g., sterol, ubiquinone, and carotenoid.

Composition and Impurities, *Yarrowia lipolytica* – Please correct: "tempaure" (add "t")

Repeated-Dose – Please state the route of exposure used in the 90-day rat study of *Saccharomyces cerevisiae* fermentate powder.

Table 6, Pichia Anomala Extract – The Totals row states the maximum concentration of use range as 0.5-0.1 (the lower value should be first), but these concentrations are not listed anywhere in the FDA product category section of the table.