

ReReview Summaries

Isobutane

Laneth Acetates

Sodium Dehydroacetate

Zinc Phenolsulfonate

EXPERT PANEL MEETING

December 4-5, 2023

Safety Assessment of Isobutane, Isopentane, Butane, and Propane as Used in Cosmetics

Status: Re-Review Summary for Panel Consideration
Release Date: November 9, 2023
Panel Meeting Date: December 4-5, 2023

History

Original Safety Assessment – published 1982

Original Re-Review – published 2005

Most Recent Action – new data considered at the September 2023 Panel meeting; not re-opened

The Expert Panel for Cosmetic Ingredient Safety members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; David E. Cohen, M.D.; Curtis D. Klaassen, Ph.D.; Allan E. Rettie, Ph.D.; David Ross, Ph.D.; Thomas J. Slaga, Ph.D.; Paul W. Snyder, D.V.M., Ph.D.; and Susan C. Tilton, Ph.D. The Cosmetic Ingredient Review (CIR) Executive Director is Bart Heldreth, Ph.D., and the Senior Director is Monice Fiume. This summary was prepared by Regina Tucker, M.S., Scientific Analyst/Writer, CIR.

ISOBUTANE, ISOPENTANE, BUTANE, and PROPANE

The Expert Panel for Cosmetic Ingredient Safety (Panel) first published the Final Report of the safety of Isobutane, Isopentane, n-Butane (now known as Butane), and Propane in 1982.¹ The Panel concluded that these ingredients are considered safe as cosmetic ingredients under the present conditions of concentration and use, as described in that safety assessment. Upon re-review in 2002, the Panel reaffirmed the original conclusion, as published in 2005.²

Because it has been at least 15 years since the prior re-review was published, in accordance with Cosmetic Ingredient Review (CIR) Procedures, the Panel again determined whether the safety assessment should be reopened. At the September 2023 meeting, the Panel reviewed updated information regarding product types and ingredient use frequencies as reported in the US Food and Drug Administration (FDA) Voluntary Cosmetic Registration Program (VCRP) database in 2023³ and maximum use concentrations provided in response to the survey conducted by the Personal Care Products Council in 2022.⁴ The frequency and concentrations of use have increased for all ingredients since the rereview was published. According to 2023 frequency of use and 2022 concentration of use data, Isobutane has the greatest frequency and concentration of use and is used in 392 formulations at up to 98% in nail products; in 2001, Butane was reported to be used in 338 formulations at up to 83% in powder products. The cumulative frequency and concentration of use data for all 4 ingredients are presented in Table 1.

In July 2023, an extensive search of the world's literature was performed for studies dated 2000 forward, and new data were found.⁵⁻¹⁷ Notably, Butane and Isobutane are listed in Annex II of the European Union (prohibited), but only if they contain $\geq 0.1\%$ butadiene. No evidence of developmental or reproductive toxicity were observed for Isobutane, Butane, or Propane, and genotoxicity studies were all negative. Irritation and sensitization studies on Isopentane were also negative. Additionally, the Panel noted that despite the very high concentrations reported for leave-on products, these ingredients are completely volatile and therefore it is expected to dissipate and not remain on the skin.

In summary, the Panel reviewed 2023 frequency and 2022 concentration of use data, in addition to new, available, relevant safety data. Considering this information, as well as the information provided in the original safety assessment and the prior re-review document, the Panel reaffirmed the 1982 conclusion for Isobutane, Isopentane, Butane, and Propane. The Panel discussed the possibility for these ingredients to be used in cosmetic products which may be incidentally inhaled. A detailed discussion and summary of the Panel's approach to evaluating incidental inhalation exposures to ingredients in cosmetic products is available at <https://www.cir-safety.org/cir-findings>.

Table 1. Frequency (2023/2001)^{2,18} and concentration (2022/2001)^{2,4} of use according to likely duration and exposure and by product category

| | Isobutane | | | | Isopentane | | | | Butane | | | | Propane | | | |
|---|---|--|------------------------------|--|----------------------------------|-------------------|---------------------|---------------------|--|---------------------|--------------------------------|--------------------------|--|---------------------|--|--|
| | # of Uses | | Max Conc of Use (%) | | # of Uses | | Max Conc of Use (%) | | # of Uses | | Max Conc of Use (%) | | # of Uses | | Max Conc of Use (%) | |
| | 2023 ¹⁸ | 2001 ² | 2022 ⁴ | 2001 ² | 2023 ¹⁸ | 2001 ² | 2022 ⁴ | 2001 ² | 2023 ¹⁸ | 2001 ² | 2022 ⁴ | 2001 ² | 2023 ¹⁸ | 2001 ² | 2022 ⁴ | 2001 ² |
| Totals* | 392 | 338 | 0.26-98 | 0.5-83 | 53 | 29 | 0.036-66.7 | 0.05-37 | 272 | 173 | 1.4-84 | 1-92 | 269 | 248 | 0.045-25.5 | 0.2-24 |
| summarized by likely duration and exposure** | | | | | | | | | | | | | | | | |
| Duration of Use | | | | | | | | | | | | | | | | |
| <i>Leave-On</i> | 246 | 212 | 0.26-98 | 0.5-83 | 6 | 2 | 0.041-66.7 | 0.05-37 | 228 | 128 | 2.6-84 | 4-92 | 171 | 158 | 0.045-25.5 | 0.2-24 |
| <i>Rinse-Off</i> | 146 | 126 | 0.53-4.5 | 0.6-38 | 46 | 27 | 0.036-2.5 | 0.05-35 | 44 | 45 | 1.4-39.9 | 1-52 | 98 | 90 | 0.65-1 | 0.4-13 |
| <i>Diluted for (Bath) Use</i> | NR | NR | NR | NR | 1 | NR | NR | NR | 0 | NR | NR | NR | NR | NR | NR | NR |
| Exposure Type | | | | | | | | | | | | | | | | |
| Eye Area | NR | NR | NR | NR | NR | NR | 66.7 | NR | NR | NR | NR | NR | NR | NR | NR | NR |
| Incidental Ingestion | NR | 5 | NR | 38 | NR | NR | NR | 35 | NR | NR | NR | NR | NR | NR | NR | NR |
| Incidental Inhalation-Spray | 88; 88 ^a ; 5 ^c | 122; 45 ^a , 4 ^c | 0.26-95, 4.1 ^a | 13-82, 0.5-38 ^a , 1-82 ^c | 1;1 ^a ;1 ^c | 1 ^c | 0.041-30 | 15; 35 ^a | 113, 55 ^a ; 8 ^c | 79, 20 ^b | 13.8-54.6; 2.6 ^a | 12-54; 4-29 ^c | 42;69 ^a , 4 ^c | 95; 22 ^a | 0.045-25.5; 1.8-12.2 ^a , | 6-21; 0.2-9 ^a ; 0.5-9 ^c |
| Incidental Inhalation-Powder | 3, 5 ^c | 4 ^c | NR | 83, 1-82 ^c | 3, 1 ^b , | 1 ^c | NR | NR | 8 ^c | NR | NR | 4-29 ^c | 4 ^c | NR | NR | 0.5-9 ^c |
| Dermal Contact | 205 | 157 | 3.4-51 | 0.5-83 | 51 | 27 | 0.036-30 | 0.05-37 | 122 | 74 | 1.9-60.6 | 1-92 | 109 | 130 | 0.75-22.9 | 0.2-21 |
| Deodorant (underarm) | 38 ^a | 20 ^a | 35-51 (aerosol) | 25-70 ^a | NR | 2 ^a | 0.95 (aerosol) | 0.5-37 ^a | 37 ^a | 5 ^a | 24.8-60.6 (aerosol) | 17-92 ^a | 38 ^a | NR | 8.3-22.9 (aerosol) | 14-16 ^a |
| Hair - Non-Coloring | 182 | 158 | 0.26-71.9 | 8-32 | 2 | NR | NR | 15 | 120 | 96 | 2.6-54.6 | 12-21 | 159 | 114 | 0.045-25.5 | 3-20 |
| Hair-Coloring | 4 | 18 | 0.53-95 | NR | NR | NR | NR | NR | 30 | 3 | 1.4-47.5 | NR | NR | 4 | 0.65 | NR |
| Nail | 1 | NR | 81.8-98 | 30 | NR | NR | NR | NR | NR | NR | 84 | NR | 1 | NR | 15 | 24 |
| Mucous Membrane | 44 | 20 | 4.5 | 2-38 | 25 | 1 | 0.036 | 0.05-35 | 10 | 12 | NR | 52 | 20 | 12 | NR | 13 |
| Baby Products | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR |
| as reported by product category | | | | | | | | | | | | | | | | |
| Bath Preparations | | | | | | | | | | | | | | | | |
| Other Bath Preparations | | | | | 1 | NR | NR | NR | | | | | | | | |
| Eye Makeup Preparations | | | | | | | | | | | | | | | | |
| Mascara | | | | | NR | NR | 66.7 | NR | | | | | | | | |
| Fragrance Preparations | | | | | | | | | | | | | | | | |
| Cologne and Toilet Water | 2 | 12 | NR | 54 | | | | | 2 | 26 | 19.2 | 29 | 1 | 17 | 7.8 | 11 |
| Perfumes | 1 | NR | NR | NR | | | | | 1 | 5 | NR | NR | | | | |
| Powders (dusting/talcum, excl aftershave talc) | NR | NR | NR | 83 | | | | | | | | | | | | |
| Sachets | NR | 4 | NR | 32 | | | | | | | | | NR | 4 | NR | NR |
| Other Fragrance Preparation | 35 | 6 | NR | 51-60 | NR | NR | 0.041 | NR | 39 | 1 | NR | 54 | 10 | 5 | 17.4 | 7-21 |
| Hair Preparations (non-coloring) | | | | | | | | | | | | | | | | |
| Hair Conditioner | 17 | 2 | NR | NR | | | | | 4 | 6 | NR | 21 | 13 | 6 | NR | 3 |
| Hair Spray (aerosol fixatives) | 46 | 107 | 0.26-71.9 (aerosol) | 13-32 | 1 | NR | NR | 15 | 41 | 47 | 22-54.6 (aerosol) | 12-14 | 31 | 72 | 0.045-25.5 (aerosol) | 6-20 |
| Shampoos (non-coloring) | 52 | NR | 1.3 (aerosol) | NR | | | | | 31 | NR | 39.9 (aerosol) | NR | 51 | NR | 0.84 (aerosol) | NR |
| Tonics, Dressings, and Other Hair Grooming Aids | 50 | 37 | 4.1 (mousse) | 8-20 | 1 | 1 | NR | NR | 32 | 19 | 2.6 | NR | 51 | 19 | 1.8-12.2 | 3-9 |
| Wave Sets | NR | 1 | NR | NR | | | | | | | | | NR | 1 | NR | NR |
| Other Hair Preparations | 17 | 11 | NR | NR | NR | 1 | NR | NR | 12 | 24 | 48 | NR | 13 | 16 | 8.8 | NR |
| Hair Coloring Preparations | | | | | | | | | | | | | | | | |
| Hair Dyes and Colors (all types requiring caution statements and patch tests) | NR | NR | 0.53 | NR | | | | | NR | NR | 1.4 | NR | NR | NR | 0.65 | NR |
| Hair Tints | NR | 17 | NR | NR | | | | | NR | 3 | NR | NR | NR | 3 | NR | NR |
| Hair Color Sprays (aerosol) | 4 | 1 | 95 (aerosol) | NR | | | | | 30 | NR | 18.4-47.5 | NR | NR | 1 | NR | NR |

Table 1. Frequency (2023/2001)^{2,18} and concentration (2022/2001)^{2,4} of use according to likely duration and exposure and by product category

| | Isobutane | | | | Isopentane | | | | Butane | | | | Propane | | | |
|---------------------------------------|--------------------|-------------------|---------------------|-------------------|--------------------|-------------------|---------------------|-------------------|--------------------|-------------------|------------------------|-------------------|--------------------|-------------------|-----------------------|-------------------|
| | # of Uses | | Max Conc of Use (%) | | # of Uses | | Max Conc of Use (%) | | # of Uses | | Max Conc of Use (%) | | # of Uses | | Max Conc of Use (%) | |
| | 2023 ¹⁸ | 2001 ² | 2022 ⁴ | 2001 ² | 2023 ¹⁸ | 2001 ² | 2022 ⁴ | 2001 ² | 2023 ¹⁸ | 2001 ² | 2022 ⁴ | 2001 ² | 2023 ¹⁸ | 2001 ² | 2022 ⁴ | 2001 ² |
| Makeup Preparations | | | | | | | | | | | | | | | | |
| Face Powders | 3 | NR | NR | NR | 3 | NR | NR | NR | | | | | | | | |
| Foundations | 3 | NR | NR | 3 | | | | | 1 | NR | NR | NR | 1 | NR | NR | 2-3 |
| Leg and Body Paints | 2 | NR | NR | NR | | | | | | | | | | | | |
| Makeup Fixatives | 1 | NR | NR | NR | | | | | 1 | NR | NR | NR | 1 | NR | NR | NR |
| Other Makeup Preparations | 1 | NR | NR | NR | | | | | | | | | | | | |
| Manicuring Preparations (Nail) | | | | | | | | | | | | | | | | |
| Basecoats and Undercoats | NR | NR | NR | 30 | | | | | | | | | NR | NR | NR | 24 |
| Other Manicuring Preparations | 1 | NR | 98 81.8(spray) | NR | | | | | NR | NR | 84 | NR | 1 | NR | 15 | NR |
| Oral Hygiene Products | | | | | | | | | | | | | | | | |
| Mouthwashes and Breath Fresheners | NR | 5 | NR | 38 | NR | NR | NR | 35 | | | | | | | | |
| Personal Cleanliness Products | | | | | | | | | | | | | | | | |
| Bath Soaps and Detergents | 36 | NR | 4.5 | NR | 24 | NR | 0.036 | NR | 1 | NR | NR | NR | 13 | NR | NR | NR |
| Deodorants (underarm) | 38 | 20 | 35-51 (aerosol) | 25-70 | NR | NR | 0.95 (aerosol) | 0.5-37 | 37 | 5 | 24.8-60.6 (aerosol) | 17-92 | 38 | 21 | 8.3-22.9 (aerosol) | 14-16 |
| Feminine Deodorants | 2 | 2 | NR | NR | | | | | 6 | NR | NR | NR | 2 | NR | NR | NR |
| Other Personal Cleanliness Products | 6 | 13 | NR | 2-16 | NR | 1 | NR | 0.05 | 3 | 12 | NR | 52 | 5 | 12 | NR | 13 |
| Shaving Preparations | | | | | | | | | | | | | | | | |
| Aftershave Lotion | NR | 6 | NR | NR | | | | | | | | | | | | |
| Mens Talcum | | | | | | | | | NR | NR | 1.9-2.3 | NR | | | | |
| Shaving Cream | 15 | 67 | 3-4.2 | 0.6-5 | 8 | 6 | 2.5 | 1-5 | 1 | 24 | NR | 1-5 | 7 | 66 | 0.75-1 | 0.4-4 |
| Shaving Soap | 3 | NR | NR | NR | 3 | NR | NR | NR | | | | | | | | |
| Other Shaving Preparations | 11 | 19 | NR | 5 | 11 | 19 | NR | NR | | | | | NR | NR | NR | 0.8 |
| Skin Care Preparations | | | | | | | | | | | | | | | | |
| Cleansing | 3 | 2 | NR | 0.9 | NR | 1 | NR | NR | 3 | NR | NR | NR | 6 | 1 | 0.8 | 2 |
| Depilatories | 3 | NR | NR | 4 | | | | | 1 | NR | NR | NR | 3 | NR | NR | 1 |
| Face and Neck (exc shave) | 1 | 1 | NR | 5 | 1 | NR | NR | NR | | | | | | | | 2 |
| Body and Hand (exc shave) | 2 | 1 | 8-9.2 (spray) | 1-75 | NR | NR | 0.55 (spray) | NR | 2 | NR | 13.8-30 (spray) | 4-29 | 2 | NR | 8.3-10.4 (spray) | 0.5-9 |
| Foot Powders and Sprays | NR | 2 | NR | 26-82 | | | | | NR | NR | 43.2 (spray) | NR | NR | NR | 18.9 (spray) | NR |
| Moisturizing | 28 | 1 | NR | 0.5-6 | | | | | 16 | NR | NR | NR | 14 | 1 | NR | 0.2-0.4 |
| Skin Fresheners | 2 | NR | NR | 21 | | | | | 2 | NR | NR | NR | 1 | NR | NR | 0.8 |
| Other Skin Care Preparations | 2 | NR | NR | 2-24 | | | | | 1 | NR | NR | 55 | 2 | NR | NR | 2-7 |
| Suntan Preparations | | | | | | | | | | | | | | | | |
| Suntan Gels, Creams, and Liquids | 1 | NR | 30 (aerosol) | NR | NR | NR | 30 (aerosol) | NR | 1 | NR | 19.4-40 (aerosol) | NR | NR | NR | 8.1 (spray) | NR |
| Indoor Tanning Preparations | 2 | 2 | NR | NR | | | | | 2 | 1 | NR | NR | 2 | 2 | NR | NR |
| Other Suntan Preparations | 2 | NR | NR | NR | | | | | 2 | NR | NR | NR | 1 | NR | NR | 1 |

NR – not reported

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

**likely duration and exposure are derived based on product category (see Use Categorization <https://www.cir-safety.org/cir-findings>)

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

^b It is possible these products are powders, but it is not specified whether the reported uses are powders.

^c Not specified whether a spray or a powder, but it is possible the use can be as a spray or a powder, therefore the information is captured in both categories

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Safety Assessment of Laneth-9 Acetate and Laneth-10 Acetate as Used in Cosmetics

Status: Re-Review Summary for Panel Consideration
Release Date: November 9, 2023
Panel Meeting Date: December 4-5, 2023

History

Original Safety Assessment – published 1982

Original Re-Review – published 2005

Most Recent Action – new data considered at the September 2023 Panel meeting; not re-opened

The Expert Panel for Cosmetic Ingredient Safety members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; David E. Cohen, M.D.; Curtis D. Klaassen, Ph.D.; Allan E. Rettie, Ph.D.; David Ross, Ph.D.; Thomas J. Slaga, Ph.D.; Paul W. Snyder, D.V.M., Ph.D.; and Susan C. Tilton, Ph.D. The Cosmetic Ingredient Review (CIR) Executive Director is Bart Heldreth, Ph.D., and the Senior Director is Monice Fiume. This summary was prepared by Priya Cherian, M.S., Senior Scientific Analyst/Writer, CIR.

LANETH-9 ACETATE and LANETH-10 ACETATE

The Expert Panel for Cosmetic Ingredient Safety (Panel) first published the Final Report on the Safety Assessment of Laneth-10 Acetate Group in 1982 (this report contained both Laneth-9 Acetate and Laneth-10 Acetate).¹ The Panel concluded that these ingredients are safe for topical application to humans in the present practices of use and concentration, as stated in that report. Upon re-review in 2002, the Panel reaffirmed the original conclusion, as published in 2005.² These two ingredients were originally reviewed with three other ingredients (Laneth-5, Laneth-16, and Laneth-25); however, these other three ingredients are not being reviewed herein as they have been included in the Alkyl PEG Ethers report.

Because it has been at least 15 years since the prior re-review was published, in accordance with Cosmetic Ingredient Review (CIR) Procedures, the Panel again determined whether the safety assessment should be reopened. At the September 2023 meeting, the Panel considered updated information regarding product types and ingredient use frequencies as reported in the US Food and Drug Administration (FDA) Voluntary Cosmetic Registration Program (VCRP) database in 2023³ and maximum use concentrations provided in response to the survey conducted by the Personal Care Products Council in 2022.⁴ In 2001, Laneth-10 Acetate was reported to be used in 44 formulations, but concentration of use data were not reported. Additionally, no uses were reported for Laneth-9 Acetate in either the VCRP or the concentration of use survey. Currently, Laneth-9 Acetate and Laneth-10 Acetate have no reported uses, according to 2022 concentration of use and 2023 FDA VCRP data. The cumulative frequency and concentration of use data for Laneth-10 Acetate are presented in Table 1. Because Laneth-9 Acetate had no previous (2001) or current (2022/2023) reported uses, it has not been included in the use table.

In July 2023, an extensive search of the world's literature was performed for studies dated 2000 forward, and no relevant new data were found.

In summary, the Panel reviewed 2023 frequency and 2022 concentration of use data and noted the lack of any new, available, relevant safety data. Considering this information, as well as the information provided in the original safety assessment and the prior re-review document, the Panel reaffirmed the 1982 conclusion.

Table 1. Frequency (2023/2001) and concentration (2022/2001) of use of Laneth-10 Acetate according to likely duration and exposure and by product category

| | # of Uses | | Max Conc of Use (%) | |
|---|-------------------|------------------------------------|---------------------|-------------------|
| | 2023 ³ | 2001 ² | 2022 ⁴ | 2001 ² |
| Totals* | NR | 44 | NR | NR |
| summarized by likely duration and exposure** | | | | |
| Duration of Use | | | | |
| Leave-On | NR | 27 | NR | NR |
| Rinse-Off | NR | 17 | NR | NR |
| Diluted for (Bath) Use | NR | NR | NR | NR |
| Exposure Type | | | | |
| Eye Area | NR | NR | NR | NR |
| Incidental Ingestion | NR | NR | NR | NR |
| Incidental Inhalation-Spray | NR | 5; 2 ^a ; 9 ^b | NR | NR |
| Incidental Inhalation-Powder | NR | 9 ^b | NR | NR |
| Dermal Contact | NR | 35 | NR | NR |
| Deodorant (underarm) | NR | NR | NR | NR |
| Hair - Non-Coloring | NR | 8 | NR | NR |
| Hair-Coloring | NR | NR | NR | NR |
| Nail | NR | 1 | NR | NR |
| Mucous Membrane | NR | 11 | NR | NR |
| Baby Products | NR | 2 | NR | NR |
| as reported by product category | | | | |
| Baby Products | | | | |
| Other Baby Products | NR | 2 | NR | NR |
| Hair Preparations (non-coloring) | | | | |
| Hair Spray (aerosol fixatives) | NR | 5 | NR | NR |
| Shampoos (non-coloring) | NR | 2 | NR | NR |
| Tonics, Dressings, and Other Hair Grooming Aids | NR | 1 | NR | NR |
| Makeup Preparations | | | | |
| Foundations | NR | 3 | NR | NR |
| Makeup Bases | NR | 1 | NR | NR |
| Manicuring Preparations (Nail) | | | | |
| Nail Polish and Enamel Removers | NR | 1 | NR | NR |
| Personal Cleanliness Products | | | | |
| Bath Soaps and Detergents | NR | 7 | NR | NR |
| Other Personal Cleanliness Products | NR | 4 | NR | NR |
| Shaving Preparations | | | | |
| Aftershave Lotion | NR | 3 | NR | NR |
| Skin Care Preparations | | | | |
| Cleansing | NR | 3 | NR | NR |
| Body and Hand (exc shave) | NR | 9 | NR | NR |
| Skin Fresheners | NR | 1 | NR | NR |
| Other Skin Care Preparations | NR | 2 | NR | NR |

NR – not reported

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

**likely duration and exposure are derived based on product category (see Use Categorization <https://www.cir-safety.org/cir-findings>)^a It is possible these products are sprays, but it is not specified whether the reported uses are sprays.^b Not specified whether a spray or a powder, but it is possible the use can be as a spray or a powder, therefore the information is captured in both categories

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- Andersen FA (ed). Final Report on the Safety Assessment of Laneth-10 Acetate Group. *J Am Coll Toxicol*. 1982;1(4).
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- Personal Care Products Council. 2022. Concentration of Use by FDA Product Category: Laneth-9 Acetate and Laneth-10 Acetate. (Unpublished data submitted by Personal Care Products Council on October 31, 2022.)

Safety Assessment of Sodium Dehydroacetate and Dehydroacetic Acid as Used in Cosmetics

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Panel Meeting Date: December 4-5, 2023

History

Original Safety Assessment – published 1985

Original Re-Review – published 2006

Most Recent Action – new data considered at the September 2023 Panel meeting; not re-opened

The Expert Panel for Cosmetic Ingredient Safety members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; David E. Cohen, M.D.; Curtis D. Klaassen, Ph.D.; Allan E. Rettie, Ph.D.; David Ross, Ph.D.; Thomas J. Slaga, Ph.D.; Paul W. Snyder, D.V.M., Ph.D.; and Susan C. Tilton, Ph.D. The Cosmetic Ingredient Review (CIR) Executive Director is Bart Heldreth, Ph.D., and the Senior Director is Monice Fiume. This summary was prepared by Priya Cherian, M.S., Senior Scientific Analyst/Writer, CIR.

SODIUM DEHYDROACETATE and DEHYDROACETIC ACID

The Expert Panel for Cosmetic Ingredient Safety (Panel) first published the Final Report on the Safety Assessment of Sodium Dehydroacetate and Dehydroacetic Acid in 1985.¹ The Panel concluded that Sodium Dehydroacetate and Dehydroacetic Acid are safe as used in the present practices of use and concentration, as stated in that report. Upon re-review in 2003, the Panel reaffirmed the original conclusion, as published in 2006.²

Because it has been at least 15 years since the prior re-review was published, in accordance with Cosmetic Ingredient Review (CIR) Procedures, the Panel again determined whether the safety assessment should be reopened. At the September 2023 meeting, the Panel considered updated 2023 information regarding product types and ingredient use frequencies as reported in the US Food and Drug Administration (FDA) Voluntary Cosmetic Registration Program (VCRP) database³ and maximum use concentrations provided in response to the survey conducted by the Personal Care Products Council.⁴ According to 2023 FDA VCRP data, the number of uses of both Sodium Dehydroacetate and Dehydroacetic Acid have increased significantly since the previous re-review. Sodium Dehydroacetate and Dehydroacetic Acid were previously reported to be used in 325 and 88 formulations in 2002, respectively, and are now reported to be used in 1233 and 833 formulations, respectively. The 2023 reported concentrations of use for both ingredients (maximum concentrations of 0.6% for Sodium Dehydroacetate and 0.7% for Dehydroacetic Acid) are the same maximum concentrations as reported in 2003. The cumulative frequency and concentrations of use data are presented in Table 1.

In July 2023, an extensive search of the world's literature was performed for studies dated 2000 forward, and new data were found.⁵⁻¹⁷ The Panel noted the cases of hypersensitivity followed by topical application of creams containing Sodium Dehydroacetate (cream reported to contain 3% Sodium Dehydroacetate in one study). Concern was mitigated due to the minimal number of case reports, in comparison to the widespread use of these ingredients, and low concentrations of use. In addition, the Panel noted the photoisomerization study, and determined that these ingredients are not likely to cause phototoxicity/ photosensitization at concentrations used in cosmetics, as supported by the existing negative phototoxicity/photosensitization data present in the original report.

In summary, the Panel reviewed 2023 frequency and concentration of use data, in addition to any new, available, relevant safety data. Considering this information, as well as the information provided in the original safety assessment and the prior re-review document, the Panel reaffirmed the 1985 conclusion. The Panel discussed the possibility for these ingredients to be used in cosmetic products which may be incidentally inhaled. A detailed discussion and summary of the Panel's approach to evaluating incidental inhalation exposures to ingredients in cosmetic products is available at <https://www.cir-safety.org/cir-findings>.

Table 1. Frequency (2023/2002) and concentration (2023/2003) of use according to likely duration and exposure and by product category

| | Sodium Dehydroacetate | | | | Dehydroacetic Acid | | | |
|---|--|-----------------------------------|---|--|---|-----------------------------------|---|---|
| | # of Uses | | Max Conc of Use (%) | | # of Uses | | Max Conc of Use (%) | |
| | 2023 ³ | 2002 ² | 2023 ⁴ | 2003 ² | 2023 ³ | 2002 ² | 2023 ⁴ | 2003 ² |
| Totals* | 1233 | 325 | 0.000005 – 0.6 | 0.00003 – 0.6 | 833 | 88 | 0.0000029 – 0.7 | 0.007 – 0.7 |
| summarized by likely duration and exposure** | | | | | | | | |
| Duration of Use | | | | | | | | |
| Leave-On | 1191 | 293 | 0.000005 – 0.6 | 0.00003 – 0.6 | 637 | 68 | 0.0000029 – 0.5 | 0.01 – 0.7 |
| Rinse-Off | 42 | 32 | 0.00003 – 0.2 | 0.0001 – 0.3 | 190 | 19 | 0.0000042 – 0.7 | 0.007 – 0.1 |
| Diluted for (Bath) Use | NR | NR | NR | NR | 6 | 1 | NR | NR |
| Exposure Type | | | | | | | | |
| Eye Area | 331 | 110 | 0.0015- 0.6 | 0.0006 – 0.5 | 145 | 9 | 0.015 – 0.5 | 0.1 – 0.3 |
| Incidental Ingestion | 5 | 1 | 0.2 – 0.5 | 0.3 – 0.5 | 61 | NR | 0.064 | NR |
| Incidental Inhalation-Spray | 3; 469 ^a ; 96 ^b | 52 ^a ; 24 ^b | 0.000005 ^a | 0.001 – 0.5 ^a 0.001 – 0.5 ^a ; 0.00003 – 0.5 ^b | 4; 131 ^a ; 166 ^b | 18 ^a ; 20 ^b | 0.0000029 – 0.000008; 0.0000042 – 0.64 ^a ; 0.062 ^b | 0.03 – 0.2 ^a ; 0.01 – 0.08 ^b |
| Incidental Inhalation-Powder | 83; 96 ^b ; 2 ^c | 34; 24 ^b | 0.2 – 0.5; 0.0005 – 0.6 ^c | 0.05 – 0.4; 0.00003 – 0.5 ^b ; 0.6 ^c | 24; 166 ^b ; 2 ^c | 3; 20 ^b | 0.0019 – 0.5; 0.062 ^b ; 0.00008 – 0.048 ^c | 0.7; 0.01 – 0.08 ^b |
| Dermal Contact | 1152 | 293 | 0.00004 – 0.6 | 0.00003 – 0.6 | 690 | 85 | 0.000021 – 0.7 | 0.007 – 0.7 |
| Deodorant (underarm) | NR | 2 ^a | 0.00004 | NR | 5 ^a | NR | NR | NR |
| Hair - Non-Coloring | 31 | 7 | 0.000005 – 0.05 | 0.2 | 76 | 1 | 0.0000029 – 0.08 | 0.02 – 0.03 |
| Hair-Coloring | NR | 3 | 0.1 | NR | NR | NR | 0.00003 | NR |
| Nail | 2 | 5 | NR | 0.02 – 0.2 | NR | 2 | NR | NR |
| Mucous Membrane | 9 | 3 | 0.00058 – 0.5 | 0.0001 – 0.3 | 99 | 1 | 0.000043 – 0.85 | 0.03 |
| Baby Products | 2 | NR | 0.05 – 0.5 | 0.6 | 7 | NR | 0.048 – 0.071 | NR |
| as reported by product category | | | | | | | | |
| Baby Products | | | | | | | | |
| Baby Shampoos | NR | NR | 0.05 | NR | 3 | NR | NR | NR |
| Baby Lotions/Oils/Powders/Creams | 2 | 0.48 | NR | 0.6 | 2 | NR | 0.048 | NR |
| Other Baby Products | NR | 0.071 | 0.5 | NR | 2 | NR | 0.071 | NR |
| Bath Preparations (diluted for use) | | | | | | | | |
| Bath Oils, Tablets, and Salts | NR | NR | NR | NR | NR | 1 | NR | NR |
| Bubble Baths | NR | NR | NR | NR | 5 | NR | NR | NR |
| Other Bath Preparations | NR | NR | NR | NR | 1 | NR | NR | NR |
| Eye Makeup Preparations | | | | | | | | |
| Eyebrow Pencil | 3 | NR | NR | 0.2 – 0.3 | 3 | NR | NR | NR |
| Eyeliner | 36 | 4 | 0.34 – 0.51 | 0.05 – 0.5 | 3 | NR | 0.15 | 0.1 |
| Eye Shadow | 204 | 74 | 0.3 – 0.6 | 0.05 – 0.3 | 99 | 4 | 0.05 – 0.5 | 0.3 |
| Eye Lotion | 8 | 3 | 0.0015 – 0.2 | NR | 16 | NR | 0.1 | 0.2 |
| Eye Makeup Remover | 1 | 1 | NR | 0.05 | 4 | 5 | 0.084 | 0.1 |
| Mascara | 43 | 16 | 0.3 – 0.5 | 0.001 – 0.4 | 5 | NR | 0.015 – 0.02 | 0.2 |
| Other Eye Makeup Preparations | 36 | 12 | 0.32 – 0.45 | 0.0006 – 0.4 | 15 | NR | NR | NR |
| Fragrance Preparations | | | | | | | | |
| Cologne and Toilet Water | 1 | NR | NR | 0.001 – 0.5 | NR | NR | NR | NR |
| Powders (dusting/talcum, excl aftershave talc) | NR | 3 | NR | NR | NR | NR | NR | NR |
| Other Fragrance Preparation | 2 | NR | NR | NR | 3 | NR | NR | NR |
| Hair Preparations (non-coloring) | | | | | | | | |
| Hair Conditioner | 10 | NR | 0.00003 – 0.015 | 0.2 | 27 | NR | 0.0000042 – 0.08 | NR |
| Hair Spray (aerosol fixatives) | NR | NR | NR | NR | 1 | NR | 0.0000029 - 0.000008 | NR |
| Shampoos (non-coloring) | 8 | 2 | 0.00003 – 0.0005 | 0.2 | 33 | NR | 0.000007 – 0.079 | 0.02 – 0.03 |
| Tonics, Dressings, and Other Hair Grooming Aids | 5 | 1 | 0.000005 | NR | 5 | 1 | 0.0000042 – 0.064 | NR |
| Other Hair Preparations | 2 | 4 | NR | NR | 6 | NR | 0.048 – 0.08 | NR |
| Hair Coloring Preparations | | | | | | | | |
| Hair Dyes and Colors (all types requiring caution statements and patch tests) | NR | NR | 0.1 | NR | NR | NR | 0.00003 | NR |
| Hair Tints | NR | 12 | NR | NR | NR | 1 | NR | NR |
| Other Hair Coloring Preparation | NR | 2 | NR | NR | NR | 2 | NR | NR |
| Makeup Preparations | | | | | | | | |
| Blushers (all types) | 69 | 15 | 0.3 – 0.45 | 0.1 – 0.4 | 31 | 1 | NR | 0.05 – 0.2 |
| Face Powders | 83 | 31 | 0.2 – 0.5 | 0.05 – 0.4 | 24 | 3 | 0.5 | 0.7 |
| Foundations | 70 | 10 | 0.00049 – 0.5 | 0.0001 – 0.4 | 1 | 3 | NR | 0.1 |
| Leg and Body Paints | NR | NR | NR | 0.1 | NR | NR | NR | NR |
| Lipstick | 5 | 1 | 0.2 – 0.5 | 0.3 | 60 | NR | 0.064 | NR |
| Makeup Bases | 5 | 6 | 0.00049 | 0.1 | 2 | NR | NR | NR |
| Rouges | 1 | NR | 0.35 | NR | NR | 1 | NR | NR |

Table 1. Frequency (2023/2002) and concentration (2023/2003) of use according to likely duration and exposure and by product category

| | Sodium Dehydroacetate | | | | Dehydroacetic Acid | | | |
|---------------------------------------|-----------------------|-------------------|---------------------|-------------------|--------------------|-------------------|---------------------|-------------------|
| | # of Uses | | Max Conc of Use (%) | | # of Uses | | Max Conc of Use (%) | |
| | 2023 ³ | 2002 ² | 2023 ⁴ | 2003 ² | 2023 ³ | 2002 ² | 2023 ⁴ | 2003 ² |
| Makeup Fixatives | NR | 1 | NR | NR | 1 | NR | NR | NR |
| Other Makeup Preparations | 15 | 4 | 0.45 | 0.0003 – 0.2 | 27 | NR | NR | 0.07 |
| Manicuring Preparations (Nail) | | | | | | | | |
| Basecoats and Undercoats | NR | NR | NR | 0.02 | NR | NR | NR | NR |
| Cuticle Softeners | NR | 2 | NR | NR | NR | 1 | NR | NR |
| Nail Creams and Lotions | NR | 3 | NR | NR | NR | NR | NR | NR |
| Nail Polish and Enamel | 1 | NR | NR | 0.2 | NR | 1 | NR | NR |
| Other Manicuring Preparations | 1 | NR | NR | 0.2 | NR | NR | NR | NR |
| Oral Hygiene Products | | | | | | | | |
| Other Oral Hygiene Products | NR | NR | NR | NR | 1 | NR | NR | NR |
| Personal Cleanliness Products | | | | | | | | |
| Bath Soaps and Detergents | 2 | 2 | 0.00058 | 0.0001 | 16 | NR | 0.000043 – 0.07 | 0.03 |
| Deodorants (underarm) | NR | 2 | 0.00004 | NR | 5 | NR | NR | NR |
| Douches | NR | NR | NR | NR | 1 | NR | NR | NR |
| Feminine Deodorants | NR | NR | NR | NR | NR | NR | 0.062 | NR |
| Other Personal Cleanliness Products | 2 | NR | NR | NR | 15 | NR | 0.064 – 0.085 | 0.03 |
| Shaving Preparations | | | | | | | | |
| Aftershave Lotion | 5 | 1 | NR | 0.0003 | 1 | NR | 0.000066 | NR |
| Beard Softeners | NR | NR | NR | NR | 2 | NR | NR | NR |
| Shaving Cream | 4 | 4 | NR | NR | 1 | NR | 0.000024 – 0.003 | NR |
| Other Shaving Preparations | NR | 1 | NR | NR | NR | NR | NR | NR |
| Skin Care Preparations | | | | | | | | |
| Cleansing | 8 | 13 | 0.0003 – 0.2 | 0.0003 – 0.3 | 65 | 8 | NR | 0.007 – 0.02 |
| Face and Neck (exc shave) | 96 | 4 | 0.0005 – 0.5 | 0.008 – 0.2 | 102 | 11 | NR | 0.01 – 0.08 |
| Body and Hand (exc shave) | 19 | 20 | 0.3 – 0.6 | 0.00003 – 0.5 | 64 | 9 | NR | 0.03 – 0.05 |
| Moisturizing | 455 | 39 | 0.1 | 0.001 – 0.3 | 96 | 10 | NR | NR |
| Night | 5 | 5 | NR | 0.003 – 0.2 | 20 | 20 | NR | 0.03 |
| Paste Masks (mud packs) | 1 | 6 | 0.00027 – 0.1 | 0.03 – 0.2 | 23 | 6 | NR | NR |
| Skin Fresheners | 4 | 2 | NR | NR | 7 | NR | NR | NR |
| Other Skin Care Preparations | 15 | 25 | NR | 0.00003 – 0.1 | 31 | 16 | NR | 0.03 |
| Suntan Preparations | | | | | | | | |
| Suntan Gels, Creams, and Liquids | NR | 1 | 0.01 – 0.05 | 0.2 | 2 | NR | 0.05 | 0.2 |
| Indoor Tanning Preparations | NR | 2 | NR | 0.4 | NR | 5 | NR | NR |
| Other Suntan Preparations | NR | 2 | 0.5 | 0.1 | 1 | NR | NR | NR |

NR – not reported

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

**likely duration and exposure are derived based on product category (see Use Categorization <https://www.cir-safety.org/cir-findings>)^a It is possible these products are sprays, but it is not specified whether the reported uses are sprays.^b Not specified whether a spray or a powder, but it is possible the use can be as a spray or a powder, therefore the information is captured in both categories^c It is possible these products are powders, but it is not specified whether the reported uses are powders.

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Safety Assessment of Zinc Phenolsulfonate as Used in Cosmetics

Status: Re-Review Summary for Panel Consideration
Release Date: November 9, 2023
Panel Meeting Date: December 4-5, 2023

History

Original Safety Assessment – published 1986

Original Re-Review – published 2006

Most Recent Action – new data considered at the September 2023 Panel meeting; not re-opened

The Expert Panel for Cosmetic Ingredient Safety members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; David E. Cohen, M.D.; Curtis D. Klaassen, Ph.D.; Allan E. Rettie, Ph.D.; David Ross, Ph.D.; Thomas J. Slaga, Ph.D.; Paul W. Snyder, D.V.M., Ph.D.; and Susan C. Tilton, Ph.D. The Cosmetic Ingredient Review (CIR) Executive Director is Bart Heldreth, Ph.D., and the Senior Director is Monice Fiume. This summary was prepared by Regina Tucker, M.S., Scientific Analyst/Writer, CIR.

ZINC PHENOLSULFONATE

The Expert Panel for Cosmetic Ingredient Safety (Panel) first published the Final Report on the Safety of Zinc Phenolsulfonate in 1986.¹ The Panel concluded that Zinc Phenolsulfonate is safe as a cosmetic ingredient in the present practices of use and concentration as described in that safety assessment. Upon re-review in 2004, the Panel reaffirmed the original conclusion, as published in 2006.²

Because it has been at least 15 years since the prior re-review was published, in accordance with Cosmetic Ingredient Review (CIR) Procedures, the Panel again determined whether the safety assessment should be reopened. At its September 2023 meeting, the Panel reviewed updated (2023) information regarding product types and ingredient use frequency as reported in the US Food and Drug Administration (FDA) Voluntary Cosmetic Registration Program (VCRP) database³ and maximum use concentrations provided in response to the survey conducted by the Personal Care Products Council.⁴ According to these data, the frequency and concentrations of use of Zinc Phenolsulfonate have decreased. In 2023, Zinc Phenolsulfonate is reported to be used in 1 formulation; however, concentration of use data were reported for several product categories, with a maximum leave-on concentration of 1% in deodorant pump spray products. In 2002, Zinc Phenolsulfonate was reported to be used in 23 formulations, and according to 2004 concentration of use data, it was used at up to 4% in deodorant formulations. The cumulative frequency and concentration of use data are presented in Table 1.

In July 2023, an extensive search of the world's literature was performed for studies dated 2001 forward, and new data were found.^{5,6} Zinc Phenolsulfonate is categorized in Annex III of the European Union, i.e., the list of substances which cosmetic products must not contain except subject to the restrictions laid down. Zinc Phenolsulfonate is confined to use in deodorants, antiperspirants, and astringent lotions at a maximum concentration of 6% (as % anhydrous substance), and eye contact is to be avoided.⁵ Additionally, according to 21CFR 310.545, there are inadequate data to establish general recognition of the safety and effectiveness of Zinc Phenolsulfonate in over-the-counter (OTC) drug products.⁶

In summary, the Panel reviewed 2023 frequency and concentration of use data, in addition to new, available, relevant safety data. Considering this information, as well as the information provided in the original safety assessment and the prior re-review document, the Panel reaffirmed the 1986 conclusion. The Panel discussed the possibility for Zinc Phenolsulfonate to be used in cosmetic products which may be incidentally inhaled. A detailed discussion and summary of the Panel's approach to evaluating incidental inhalation exposures to ingredients in cosmetic products is available at <https://www.cir-safety.org/cir-findings>.

Table 1. Frequency (2023/2002) and concentration (2023/2004) of use according to likely duration and exposure and by product category

| | # of Uses | | Max Conc of Use (%) | |
|--|-------------------|---------------------------------|---------------------------------|-------------------|
| | 2023 ³ | 2002 ² | 2023 ⁴ | 2004 ² |
| Totals | 1 | 23 | 0.041-1 | 3-4 |
| summarized by likely duration and exposure* | | | | |
| Duration of Use | | | | |
| Leave-On | 1 | 23 | 0.041-1 | 3-4 |
| Rinse-Off | NR | NR | NR | NR |
| Diluted for (Bath) Use | NR | NR | 1 | NR |
| Exposure Type | | | | |
| Eye Area | NR | NR | NR | NR |
| Incidental Ingestion | NR | NR | NR | NR |
| Incidental Inhalation-Spray | NR | 1 ^a ; 3 ^b | 0.42 | 3 ^b |
| Incidental Inhalation-Powder | NR | 1; 3 ^b | 0.1-0.2 ^c | 3 ^b |
| Dermal Contact | 1 | 23 | 0.041-1 | 3-4 |
| Deodorant (underarm) | NR | 15 ^a | 0.041-1 (spray) | 4 ^a |
| Hair - Non-Coloring | NR | NR | NR | NR |
| Hair-Coloring | NR | NR | NR | NR |
| Nail | NR | NR | NR | NR |
| Mucous Membrane | NR | NR | 1 | NR |
| Baby Products | NR | NR | NR | NR |
| as reported by product category | | | | |
| Bath Preparations | | | | |
| Bath Oils, Tablets, and Salts | NR | NR | 1 | NR |
| Fragrance Preparations | | | | |
| Powders (dusting and talcum, exc aftershave talc) | NR | 1 | NR | NR |
| Personal Cleanliness | | | | |
| Deodorants (underarm) | NR | 15 | 0.041 (spray) 1 (pump spray) | 4 |
| Shaving Preparations | | | | |
| Aftershave Lotion | NR | 2 | NR | NR |
| Skin Care Preparations | | | | |
| Face and Neck (exc shave) | NR | NR | 0.2 (not spray) | NR |
| Body and Hand (exc shave) | NR | 2 | 0.1 (not spray) 0.42 (spray) | NR |
| Foot Powders and Sprays | NR | 1 | NR | 3 |
| Moisturizing | NR | 1 | NR | NR |
| Other Skin Care Preparations | 1 | 1 | 0.25 | NR |

NR – not reported

*likely duration and exposure are derived based on product category (see Use Categorization <https://www.cir-safety.org/cir-findings>)^a It is possible these products are sprays, but it is not specified whether the reported uses are sprays.^b Not specified whether a spray or a powder, but it is possible the use can be as a spray or a powder, therefore the information is captured in both categories^c It is possible these products are powders, but it is not specified whether the reported uses are powders.

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