Safety Assessment of Tris(Tetramethylhydroxypiperidinol) Citrate as Used in Cosmetics

Status: Scientific Literature Review for Public Comment
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All interested persons are provided 60 days from the above release date (February 16, 2020) to comment on this safety assessment and to identify additional published data that should be included or provide unpublished data which can be made public and included. Information may be submitted without identifying the source or the trade name of the cosmetic product containing the ingredient. All unpublished data submitted to CIR will be discussed in open meetings, will be available at the CIR office for review by any interested party and may be cited in a peer-reviewed scientific journal. Please submit data, comments, or requests to the CIR Executive Director, Dr. Bart Heldreth.

INTRODUCTION

This Scientific Literature Review is the initial step in preparing a safety assessment of Tris(Tetramethylhydroxypiperidinol) Citrate as used in cosmetic formulations. According to the web-based International Cosmetic Ingredient Dictionary and Handbook (wINCI; Dictionary), Tris(Tetramethylhydroxypiperidinol) Citrate is reported to function in cosmetics as a light stabilizer.1

This safety assessment includes relevant published and unpublished data that are available for each endpoint that is evaluated. Published data are identified by conducting an exhaustive search of the world’s literature. A listing of the search engines and websites that are used and the sources that are typically explored, as well as the endpoints that CIR typically evaluates, is provided on the CIR website (https://www.cir-safety.org/supplementaldoc/preliminary-search-engines-and-websites; https://www.cir-safety.org/supplementaldoc/cir-report-format-outline). Unpublished data are provided by the cosmetics industry, as well as by other interested parties.

Much of the data included in this safety assessment was found on the European Chemicals Agency (ECHA) website.2 Please note that the ECHA website provides summaries of information generated by industry, and it is those summary data that are reported in this safety assessment when ECHA is cited.

CHEMISTRY

Definition and Structure

Tris(Tetramethylhydroxypiperidinol) Citrate (CAS No. 220410-74-2) is the salt that conforms to the structure shown in Figure 1.1

![Figure 1. Tris(Tetramethylhydroxypiperidinol) Citrate](image)

Physical and Chemical Properties

Tris(Tetramethylhydroxypiperidinol) Citrate is soluble in water3 and exhibits a high topological polar surface area of 263 Å².3 The physical and chemical properties of Tris(Tetramethylhydroxypiperidinol) Citrate are further outlined in Table 1. Particle size distribution is presented in Table 2.

Method of Manufacture

Method of manufacture data were not found in the published literature, and unpublished data were not submitted.

Impurities

Impurities data were not found in the published literature, and unpublished data were not submitted.

USE

Cosmetic

The safety of the cosmetic ingredient addressed in this assessment is evaluated based on data received from the US Food and Drug Administration (FDA) and the cosmetics industry on the expected use of this ingredient in cosmetics. Use frequencies of individual ingredient in cosmetics is collected from manufacturers and reported by cosmetic product category in the FDA Voluntary Cosmetic Registration Program (VCRP) database. Use concentration data are submitted by the
cosmetic industry in response to a survey, conducted by the Personal Care Products Council (Council), of maximum reported use concentrations by product category.

According to 2019 VCRP survey data, Tris(Tetramethylhydroxypiperidinol) Citrate is reported to be used in 379 formulations, mostly used in leave-on formulations (329 uses; Table 3). The results of the concentration of use survey conducted by the Council indicate that Tris(Tetramethylhydroxypiperidinol) Citrate is reported to be used at a maximum use concentration of 0.05%.

Tris(Tetramethylhydroxypiperidinol) Citrate is used in formulations applied to the eye area, at up to 0.005%. It is also used in products which allow for mucous membrane exposure, at a maximum concentration of 0.05% in bath soaps and detergents. According to VCRP data, Tris(Tetramethylhydroxypiperidinol) Citrate is used in a baby product formulation; however, concentration of use data were not reported for any baby products.

Additionally, Tris(Tetramethylhydroxypiperidinol) Citrate is used in cosmetic sprays and could possibly be inhaled; for example, Tris(Tetramethylhydroxypiperidinol) Citrate is reported to be used up to 0.05% in cologne and toilet waters. In practice, 95% to 99% of the droplets/particles released from cosmetic sprays have aerodynamic equivalent diameters > 10 µm, with propellant sprays yielding a greater fraction of droplets/particles < 10 µm compared with pump sprays. Therefore, most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and thoracic regions of the respiratory tract and would not be respirable (i.e., they would not enter the lungs) to any appreciable amount.

Tris(Tetramethylhydroxypiperidinol) Citrate is not restricted from use in any way under the rules governing cosmetic products in the European Union.

Non-Cosmetic

Non-cosmetic uses were not found in the published literature, and unpublished data were not submitted.

TOXICOKINETIC STUDIES

Toxicokinetic studies were not found in the published literature, and unpublished data were not submitted. However, the following presumptions regarding absorption, distribution, metabolism and excretion are based on physical and chemical properties of Tris(Tetramethylhydroxypiperidinol) Citrate.

After oral administration, Tris(Tetramethylhydroxypiperidinol) Citrate will likely dissolve in the gastrointestinal fluids, as indicated by the high water solubility. Since absorption of weak acidic compounds is favored at low pH values, uptake of the minor compound (not specified) in the stomach is expected. Due to its high pKa value (~11), the main component (not specified) is assumed to be ionic under the pH conditions of the stomach (pH ~1) and the intestine (pH 7-8); therefore, absorption via aqueous pores or carriage across membranes with the bulk passage of water might occur.

Due to the solid properties of the test substance, inhalation of dust might occur. The aerodynamic diameter of the particles has been shown to be approximately 5 µm. Due to high water solubility, Tris(Tetramethylhydroxypiperidinol) Citrate will likely dissolve into the mucus where it might be retained and transported out of the respiratory tract. It is not expected that Tris(Tetramethylhydroxypiperidinol) Citrate will penetrate the skin.

TOXICOLOGICAL STUDIES

Acute Toxicity Studies

Dermal

An acute dermal toxicity study was performed in accordance with Organization for Economic Co-operation and Development (OECD) test guideline (TG) 402. A group of 5 male and 5 female New Zealand White rabbits received a single dermal administration of Tris(Tetramethylhydroxypiperidinol) Citrate (93.64% pure); the application covered approximately 10% of the body surface area. The rabbits were exposed to an occlusive patch of the substance in deionized water (1 mL of deionized water/g of test substance) at a dose of 2000 mg/kg bw (or 2136 mg/kg bw for 24 h). The rabbits were observed for mortality and clinical abnormalities 14 d before euthanization. No mortality occurred during the observation period. Clinical abnormalities included small feces, soft/mucoid stools, fecal stain, and dark material around the facial area. Dermal irritation was observed at the site of test article application. No significant gross internal findings were observed in the rabbits at necropsy. Under the conditions of this test, the acute dermal LD50 was determined to be greater than 2136 mg/kg bw.

Oral

In a single-dose oral toxicity study performed in accordance with OECD TG 401, groups of 5 male and 5 female Sprague-Dawley rats were dosed with Tris(Tetramethylhydroxypiperidinol) Citrate in deionized water by gavage. Male rats received doses of 1068, 2136, 2670, and 3204 mg/kg bw, while female rats received doses of 534, 1068, 1602, or 2136 mg/kg bw. There were no controls in this study. All study animals were observed for mortality or clinical abnormalities for 14 d
after exposure. One male dosed with 2136 mg/kg, 4 dosed with 2670 mg/kg, and all females dosed with 1602 2136 mg/kg Tris(Tetramethylhydroxyxypiperidino) Citrate, died; mortality occurred on day 1. The most notable clinical abnormalities observed during the study included decreased activity, convulsions, wobbly gait, breathing abnormalities, prostration, decreased defecation, soft stools, piloerection, apparent hypothennia, blue skin tone, hunched posture, urine/fecal stain, partially closed eyelids, salivation, dilated pupils, ocular discharge, and dark material around the facial area. Gross internal pathologies noted in animals that died prematurely included abnormal digestive tract content, stained mucosa in the stomach, and dark red lungs, while gross internal findings observed at necropsy included three incidences of gray raised area(s) on the lungs in the 2136 mg/kg bw male rats. The acute oral LD50 of the test substance in the male rat was determined to be 2495 mg/kg bw, and the oral LD50 was estimated to be between 1068 and 1602 mg/kg bw in the female rat. The oral LD50 for both sexes was determined to be 1758 mg/kg bw.

Inhalation

An acute inhalation study was conducted according to OECD TG 403 in rats. Five male and 5 female Sprague-Dawley rats were exposed nose-only for 4 h to a fine white powder, composed of 94.8%Tris(Tetramethylhydroxyxypiperidino) Citrate, 3.8% water, and 0.6% other, which was aerosolized in a gravimetric chamber at a concentration of 5.08 mg/L. The estimated mass median aerodynamic diameter (MMAD) was 3.8 µm. The animals were observed for mortality and signs of gross toxicity for 14 d after exposure, and then necropsied. All animals survived the study and no gross abnormalities were noted upon necropsy. Under the conditions of this study, the acute inhalation LC50 was determined to be greater than 5.08 mg/L in male and female rats.

Short-Term Toxicity Studies

Oral

In accordance with OECD TG 407, groups of 5 male and 5 female Sprague-Dawley rats were exposed to 0 (control), 100 (low), 500 (mid), and 1000 (high-dose) mg/kg bw/d Tris(Tetramethylhydroxyxypiperidino) Citrate in deionized water via gavage for 28 d, and then killed. Two additional groups of 5 males and 5 females were dosed with 0 or 1000 mg/kg/d for 28 d, and then observed post-exposure for 14 d, serving as recovery groups. No mortality occurred during the study. Dose-dependent abnormalities, such as salivation and apparent blood around the facial area, neck and forelimbs, were identified in the males and females dosed with 500 and 1000 mg/kg bw/d. Clinical pathology findings showed a slight increase of serum bilirubin in high-dose male rats, and a statistically significant slight decrease in red blood cell counts (RBC), hemoglobin and hematocrit in females (except for RBC at the mid dose). Spleen weights were increased in the mid- and high-dose male rats, and there was a minimal to mild increase in the congestion of red pulp of the spleen in several of the male and female rats of the high-dose group. These effects were reversible during the recovery period. The no-observed-effect-level (NOEL) was determined to be 100 mg/kg bw/d.

Subchronic Toxicity Studies

Dermal

The dermal toxicity of Tris(Tetramethylhydroxyxypiperidino) Citrate (97.3% pure) was evaluated in a 90-day study in rats, according to OECD TG 411. The test substance was administered as a suspension in 0.5% carboxymethylcellulose aqueous solution, and open applications of 0, 50, 150, or 500 mg/kg bw/d were made to the clipped skin of groups of 10 male and 10 female rats. The coverage area was approximately 10% of body surface area (i.e., 45 - 50 cm2 in males and 30 – 35 cm2 in females). The animals were killed at the termination of dosing. An additional two groups of 5 males and 5 females received open applications of 0 or 500 mg/kg bw/d of the test substance for 13 wks, and were observed for 4 wks post-dosing as recovery animals. The application sites were not wiped after dosing and were only cleaned in the instance of excess residue with purified water; ingestion was not prevented. There were no premature deaths. Scabs were noted at the application site during dosing in 2/15 males and 3/15 females dosed with 500 mg/kg bw/d and 1/10 females in both the 50 and 150 mg/kg bw/d. Chorioretinopathy, noted in 2 males and 1 female dosed with 500 mg/kg bw/d, was considered age- and strain-related, and not a test article-related adverse effect. Abberations in glucose, urea, and potassium concentrations and white blood cell count were also observed in animals given 50 and 500 mg/kg bw/d. The effect on glucose and urea were reversible; however, the effects on white blood cell count and potassium concentrations persisted. An increase in spleen weight and congestion was observed in males and females, but similar congestion was observed in the controls, and the increased weight was reversed in the 500 mg/kg bw/d group of animals following the recovery period. Minimal acanthosis of the epidermis occurred in males and females across all dosing groups, however, it was considered negligible due to similarities in controls. Based on the results of this study, the no-observed-adverse-effect-level (NOAEL) for cutaneous application of the test substance was determined to be 150 mg/kg bw/d.

GENOTOXICITY

In Vitro

The mutagenicity of Tris(Tetramethylhydroxyxypiperidino) Citrate (93.64% pure) was evaluated in Salmonella typhimurium TA 1535, TA 1537, TA 98, TA 100 and Escherichia coli WP2 uvr A, using an Ames, mammalian-microsome
reverse mutation assay with a confirmatory assay. The assay was conducted with five doses of the test article (100, 333, 1000, 3330, 5000 µg per plate) in both the presence and absence of metabolic activation. The results of this assay indicated that the test substance did not cause a positive increase in the mean number of revertants per plate with any of the tested strains either in the presence or absence of metabolic activation. Concurrent vehicle (dimethyl sulfoxide; DMSO) and appropriate positive controls gave expected results.

The ability of Tris(Tetramethylhydroxyxypiperidinol) Citrate to induce chromosomal aberrations in Chinese hamster ovary (CHO) cells, with and without metabolic activation, was tested according to OECD TG 473. The test substance was dissolved in cell culture grade water at concentrations up to 5000 µg/mL, with and without metabolic activation. Except for a weak increase in cells with chromosomal aberrations at 5000 µg/mL in the non-activation assay, no significant increase in cells with chromosomal abnormalities, polyploidy, or endoreduplication was observed.

**In Vivo**

A micronucleus assay was performed with Tris(Tetramethylhydroxyxypiperidinol) Citrate (93.64% pure), in accordance with OECD TG 474. Groups of 6 CD-1 male mice received 50, 100, or 200 mg/kg bw dosed intravenously with the test article in sterile water. A concurrent vehicle and positive control (cyclophosphamide, given orally) group was also used. Five animals from the 50 and 100 mg/kg bw dose groups and 5 animals from the positive control group were euthanized approximately 24 h after dosing for bone marrow extraction. Five animals from the 200 mg/kg bw dose group and five animals dosed of the vehicle control group were euthanized approximately 24 and 48 h after dosing for bone marrow extraction. Clinical toxicity was observed in 200 mg/kg animals, and 2 animals from this dosing group died in the 24 h harvest group. However, the test item did not induce a statistically significant increase in the frequency of micronucleated polychromatic erythrocyte sand was therefore considered non-clastogenic.

**DERMAL IRRITATION AND SENSITIZATION**

**Irritation**

**Animal**

The dermal irritation potential of aqueous Tris(Tetramethylhydroxyxypiperidinol) Citrate (93.64% pure) was evaluated in 3 male and 3 female New Zealand white rabbits, in accordance with OECD TG 404. The test article (0.5 g) was applied for 4 h to 1 in² of shaved skin using a semi-occlusive patch. The test sites were washed and dried after exposure with deionized water and gauze, and observed for up to 7 days following patch removal. A mean erythema score of 1 (maximum score of 4) and mean edema score of 0 were reported; erythema was completely reversible by day 7. Based on Regulation (EC) No. 1272/2008 (CLP), the test item was considered non-irritating based on both the erythema and edema score.

**Sensitization**

**Animal**

A guinea pig maximization test was performed in accordance to OECD TG 406. Ten male and 10 female Hartley albino guinea pigs received intradermal injections of 5.0% Tris(Tetramethylhydroxyxypiperidinol) Citrate in deionized water, along with injections of Freund’s Complete Adjuvant (FCA), and the test article in FCA. The control group (5 male and 5 female guinea pigs) received the same injections, but without the test article. On day 6, 0.5 mL of 10% w/w sodium lauryl sulfate in petrolatum was spread over the intradermal injection sites of all animals. On day 7, any residual sodium lauryl sulfate was removed, 48-h patches with undiluted test article were applied to the test animals, and deionized water was applied to the controls. Challenge applications were made with undiluted test article on day 20, using Hilltop chambers. Rechallenge applications were made 8 days later in test and control groups. Group mean dermal scores were noted to be similar in test animals compared with the challenge control animals. Tris(Tetramethylhydroxyxypiperidinol) Citrate was not considered a sensitizer.

**Human**

A modified Draize test for dermal sensitization was completed in 104 human subjects. Subjects were exposed to an occlusive patch containing 0.2 mL of 0.1% or 0.5% Tris(Tetramethylhydroxyxypiperidinol) Citrate in distilled water, for 24 h, three times per week for 3 wks. The control was distilled water or 0.1% aqueous sodium lauryl sulfate. The test site was wiped with water after each testing phase. After a rest period of 10 - 17 days, a previously unexposed site was challenged with Tris(Tetramethylhydroxyxypiperidinol) Citrate for 24 h. Three adverse events were reported during the course of the study, but they were not related to exposure to the test substance. Furthermore, the test substance did not appear to cause significant irritation potential during the 3 wk induction period or during the challenge phase of the study.
OCULAR IRRITATION

Animal

The ocular irritation potential of Tris(Tetramethylhydroxy-piperidinol) Citrate (93.64% pure) was evaluated on the eyes of 3 female New Zealand White rabbits, in accordance to OECD TG 405. One mL of undiluted test article was instilled into the conjunctival sac of the right eye, and the other eye remained untreated and served as the corresponding control for each animal. Test and control eyes were examined for signs of irritation for up to 10 days following dosing. The mean irritation score was 0.78 (maximum score of 3), and irritation was fully reversible between 72 h and 10 days of exposure. Based on Regulation (EC) No 1272/2008 (CLP) criteria, the test item was considered non-irritating to rabbit eyes.

SUMMARY

According to the Dictionary, Tris(Tetramethylhydroxy-piperidinol) Citrate is reported to function in cosmetics as a light stabilizer. It is reported to be used in 379 formulations, and the highest reported concentration of use is 0.05% in cologne and toilet waters and in bath soaps and detergents.

In an acute dermal toxicity study, 10 New Zealand White rabbits were exposed to an occlusive patch of up to 2136 mg/kg bw of Tris(Tetramethylhydroxy-piperidinol) Citrate for 24 h. The dermal LD₅₀ was determined to be greater than 2136 mg/kg bw.

In an acute oral toxicity study, 40 Sprague-Dawley rats received up to 3204 mg/kg bw (highest male dose) and 2136 mg/kg bw (highest female dose) of Tris(Tetramethylhydroxy-piperidinol) Citrate, by gavage. Three males and 2 females, who received the highest dose, died prior to scheduled necropsy. The oral LD₅₀ for both sexes was determined to be 1758 mg/kg bw.

In an acute inhalation toxicity, 10 Sprague-Dawley rats were exposed to aerosolized 94.8% pure Tris(Tetramethylhydroxy-piperidinol) Citrate (estimated MMAD 3.8 µm), at a concentration of 5.08 mg/L, nose-only, for 4 h. The acute inhalation LC₅₀ was determined to be greater than 5.08 mg/L.

In a repeated 28-d oral toxicity study, 60 Sprague-Dawley rats received up to 1000 mg/kg bw of Tris(Tetramethylhydroxy-piperidinol) Citrate via gavage. Dose-dependent clinical abnormalities observed included increased serum bilirubin, statistically significant decrease in red blood cell counts, haemoglobin, and hemocrit. Spleen weights and congestion also increased, but these effects were reversible during the recovery period. The NOEL was determined to be 100 mg/kg bw/d.

In a 13-wk dermal toxicity study, 100 Wistar Han rats were exposed to an open application of up to 500 mg/kg bw/d, 97.3% pure Tris(Tetramethylhydroxy-piperidinol) Citrate. Scabs were noted at the application site during the treatment; chorioretinopathy, aberrations in glucose, urea, white blood cell count, and potassium concentration were also observed, but were mostly reversible during the treatment-free period. Based on the results of this study, the NOAEL was determined to be 150 mg/kg bw/d.

Tris(Tetramethylhydroxy-piperidinol) Citrate was not mutagenic in the Ames test or in a chromosomal aberration assay, using CHO cells, tested at concentrations up to 5000 µg/plate. Tris(Tetramethylhydroxy-piperidinol) Citrate was not clastogenic in a mouse micronucleus assay, in which mice were intravenously dosed with up to 200 mg/kg bw of the test substance.

Undiluted Tris(Tetramethylhydroxy-piperidinol) Citrate was considered non-irritating to the skin of 6 New Zealand White rabbits following semiocclusive application to a 1 in² patch of shaved skin for 4 h; a mean erythema score of 1 and mean edema score of 0 was reported. Tris(Tetramethylhydroxy-piperidinol) Citrate was not considered a sensitizer in a guinea pig maximization test.

In clinical testing with 104 subjects, Tris(Tetramethylhydroxy-piperidinol) Citrate was not an irritant or a sensitizer.

Tris(Tetramethylhydroxy-piperidinol) Citrate was considered non-irritating to 3 New Zealand White rabbit eyes. The mean irritation score was 0.78 (maximum score of 3), and irritation was fully reversible between 72 h and 10 days.

INFORMATION SOUGHT

The CIR is seeking the following information on Tris(Tetramethylhydroxy-piperidinol) Citrate for use in the resulting safety assessment:

1. Method of manufacturing
2. Composition
3. Impurities
4. UV absorption data; if absorbed, phototoxicity/photosensitization data may be needed
5. Toxicokinetic data, particularly dermal penetration data
6. Inhalation toxicity data
### Table 1. Physical and Chemical Properties of Tris(Tetramethylhydroxypiperidinol) Citrate

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical Form (@ 20°C &amp; 1013 hPa)</td>
<td>solid</td>
<td>2</td>
</tr>
<tr>
<td>Formula Weight (g/mol)</td>
<td>711.9</td>
<td>3</td>
</tr>
<tr>
<td>Topological Polar Surface Area (Å²)</td>
<td>263</td>
<td>3</td>
</tr>
<tr>
<td>Density/Specific Gravity (g/mL @ 24 °C)</td>
<td>1.19</td>
<td>2</td>
</tr>
<tr>
<td>Vapor pressure (Pa @ 30°C)</td>
<td>&lt; 0.6</td>
<td>2</td>
</tr>
<tr>
<td>Melting Point (°C)</td>
<td>59.17-64.26</td>
<td>2</td>
</tr>
<tr>
<td>Boiling Point (°C)</td>
<td>Decomposed before boiling under nitrogen at atmospheric pressure</td>
<td>2</td>
</tr>
<tr>
<td>Partition coefficient (@ 20°C &amp; pH = 4)</td>
<td>-0.29</td>
<td>2</td>
</tr>
<tr>
<td>Water Solubility (g/L @ 20.5°C)</td>
<td>&gt; 500</td>
<td>2</td>
</tr>
</tbody>
</table>

### Table 2. Particle size distribution

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Particle size distribution/granulometry</td>
<td>79% at 2.0mm; 14% at 1.0mm; 3% at 500µm; 3% at 125µm; 1% at 75µm</td>
</tr>
</tbody>
</table>

### Table 3. Frequency (2019) and concentration (2018) of use of Tris(Tetramethylhydroxypiperidinol) Citrate

<table>
<thead>
<tr>
<th></th>
<th># of Uses</th>
<th>Max Conc of Use (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Totals*</td>
<td>379</td>
<td>0.0001-0.05</td>
</tr>
<tr>
<td><strong>Duration of Use</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leave-On</td>
<td>329</td>
<td>0.0001-0.05</td>
</tr>
<tr>
<td>Rinse-Off</td>
<td>43</td>
<td>0.005-0.05</td>
</tr>
<tr>
<td>Diluted for (Bath) Use</td>
<td>7</td>
<td>NR</td>
</tr>
<tr>
<td><strong>Exposure Type</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eye Area</td>
<td>5</td>
<td>0.005</td>
</tr>
<tr>
<td>Incidental Ingestion</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Incidental Inhalation-Spray</td>
<td>149; 137; 26</td>
<td>0.0001-0.05; 0.0001-0.01; 0.005</td>
</tr>
<tr>
<td>Incidental Inhalation-Powder</td>
<td>26; 1</td>
<td>0.005-0.01</td>
</tr>
<tr>
<td>Dermal Contact</td>
<td>364</td>
<td>0.0001-0.05</td>
</tr>
<tr>
<td>Deodorant (underarm)</td>
<td>2</td>
<td>Not spray: 0.01</td>
</tr>
<tr>
<td>Hair - Non-Coloring</td>
<td>14</td>
<td>0.0001-0.01</td>
</tr>
<tr>
<td>Hair-Coloring</td>
<td>1</td>
<td>0.005</td>
</tr>
<tr>
<td>Nail</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Mucous Membrane</td>
<td>31</td>
<td>0.01-0.05</td>
</tr>
<tr>
<td>Baby Products</td>
<td>1</td>
<td>NR</td>
</tr>
</tbody>
</table>

*Because this ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure types may not equal the sum of total uses.
1 It is possible these products are sprays, but it is not specified whether the reported uses are sprays.
2 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.
3 It is possible these products are powders, but it is not specified whether the reported uses are powders
4 NR – not reported
REFERENCES


