Safety Assessment of
Pentaerythrityl Tetra-Di-t-Butyl Hydroxyhydrocinnamate as
Used in Cosmetics

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All interested persons are provided 60 days from the above date to comment on this Tentative Report and to identify additional published data that should be included or provide unpublished data which can be made public and included.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 All unpublished data submitted to CIR will be discussed in open meetings, will be available at the CIR office for review by any interested party and may be cited in a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 Director, Dr. Lillian J. Gill.

The 2013 Cosmetic Ingredient Review Expert Panel members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; Ronald A. Hill, Ph.D.; James G. Marks, Jr., M.D.; Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; and Paul W. Snyder, D.V.M., Ph.D. The CIR Director is Lillian J. Gill, D.P.A. This report was prepared by Wilbur Johnson, Jr., M.S., Senior Scientific Analyst and Bart Heldreth, Ph.D., Chemist.
# Table of Contents

**INTRODUCTION** ............................................................................................................................... 1

**CHEMISTRY** ............................................................................................................................... 1

  - Definition and Structure ........................................................................................................... 1
  - Physical and Chemical Properties ......................................................................................... 1

**USE** .................................................................................................................................................. 2

  - Cosmetic ................................................................................................................................. 2
  - Non-Cosmetic .......................................................................................................................... 2

**TOXICOKINETICS** ......................................................................................................................... 2

**TOXICOLOGY** .................................................................................................................................. 2

  - Acute Toxicity ........................................................................................................................... 2
    - Inhalation ............................................................................................................................... 2
    - Oral ......................................................................................................................................... 3
    - Dermal ..................................................................................................................................... 3
  - Repeated Dose Toxicity ............................................................................................................. 3
    - Skin Sensitization .................................................................................................................. 3

**REPRODUCTIVE AND DEVELOPMENTAL TOXICITY** ............................................................... 3

**GENOTOXICITY** .............................................................................................................................. 4

  - In Vitro Assays .......................................................................................................................... 4
  - In Vivo Assays ............................................................................................................................ 4

**CARCINOGENICITY** ....................................................................................................................... 5

**SUMMARY** ....................................................................................................................................... 5
INTRODUCTION

This scientific literature review presents information relevant to evaluating the safety of pentaerythritol tetra-di-t-butyl hydroxyhydrocinnamate as used in cosmetics. This ingredient functions as an antioxidant in cosmetic products.

CHEMISTRY

Definition and Structure

Pentaerythritol Tetra-di-t-butyl Hydroxyhydrocinnamate (CAS No. 6683-19-8) is the cinnamate tetraester of pentaerythritol conforming to the formula:1

![Chemical Structure of Pentaerythritol Tetra-di-t-butyl Hydroxyhydrocinnamate](image)

Figure 1. Pentaerythritol Tetra-di-t-butyl Hydroxyhydrocinnamate

Physical and Chemical Properties

Chemical and physical properties of pentaerythritol tetra-di-t-butyl hydroxyhydrocinnamate are included in Table 1.2
Cosmetic

Pentaerythritol tetra-di-t-butyl hydroxyhydrocinnamate functions as an oxidant in cosmetic products. Information on the use of this ingredient as a function of product type was supplied to the Food and Drug Administration (FDA) by industry as part of the Voluntary Cosmetic Registration Program (VCRP) in 2013. The Personal Care Products Council (council) conducted a survey of ingredient use concentrations in 2013, indicating use at concentrations up to 0.8%. Ingredient frequency of use and concentration data are included in Table 2.

Cosmetic products containing pentaerythritol tetra-di-t-butyl hydroxyhydrocinnamate may be applied to the skin and hair, or, incidentally, may come in contact with the eyes and mucous membranes. Products containing this ingredient may be applied as frequently as several times per day and may come in contact with the skin or hair for variable periods following application. Daily or occasional use may extend over many years.

Pentaerythritol tetra-di-t-butyl hydroxyhydrocinnamate is used in products that are sprayed (highest maximum use concentration = 0.44%) and in powders (highest maximum use concentration = 0.014%). Additionally, it is possible that various skin care products containing this ingredient may be powders (highest maximum use concentration = 0.34%). Because these ingredients are used in products that are sprayed, they could possibly be inhaled. 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 below 10 µm, compared with pump sprays. Therefore, most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and bronchial regions and would not be respirable (i.e., they would not enter the lungs) to any appreciable amount.

Non-Cosmetic

Pentaerythritol tetra-di-t-butyl hydroxyhydrocinnamate (Tetrakis[Methylene(3,5-Di-Tert-Butyl-4-Hydroxyhydrocinnamate]Methane) has been approved by FDA for use as a component of adhesives that may be safely used as components of articles intended for use in packaging, transporting, or holding food, and as a component of resinous and polymeric coatings for food contact surfaces of such articles. According to FDA, this chemical may also be safely used as an antioxidant and/or stabilizer in polymers used in the manufacture of articles that may come in contact with food, with the following restrictions: at levels not to exceed 0.5% by weight of all polymers used as indirect additives in food packaging, except at levels of ≤ 0.1% by weight of petroleum wax or synthetic petroleum wax, or at levels of ≤ 1% by weight of petroleum alicyclic hydrocarbon resins or their hydrogenated products, of rosin and rosin derivatives, and of terpene resins. Other FDA restrictions include use as a component (antioxidant) of lubricants with incidental food contact at a level not to exceed 0.5% by weight of the lubricant, and use as a component of surface lubricants employed in the manufacture of metallic articles that contact food, at a level not to exceed 0.5% by weight of the finished surface lubricant formulation.

TOXICOKINETICS

Data on the absorption, distribution, metabolism, and excretion of pentaerythritol tetra-di-t-butyl hydroxyhydrocinnamate were not found in the published literature, nor were unpublished data provided.

TOXICOLOGY

Inhalation

In an acute inhalation toxicity study, groups of 20 rats (males and females; strain and ages not stated) were exposed, nose-only, to aerosolized pentaerythritol tetra-di-t-butyl hydroxyhydrocinnamate for 4 h. The test material was administered at a dose of 762 or 1,951 mg/m³ of air, and untreated rats served as controls. The animals were observed at 1 h, 2 h, and 4 h into the exposure period, at 2 h post-exposure, and then daily for 14 days. Gross pathologic examination was performed at the end of the observation period. None of the animals died during the 14-day observation period. Slight dyspnea and ruffled fur were observed in both dose groups, and all animals recovered within 6 days. There were no differences in body weight or body weight gain between the dose groups, and pathological changes were not observed at necropsy.
Oral

The acute oral toxicity of pentaerythritol tetra-di-t-butyl hydroxyhydrocinnamate was evaluated using groups of 4 Sprague-Dawley rats (2 males, 2 females/group; ages not stated). This study (non-GLP study) was performed by Industrial Bio-Test Labs, Inc. The test material (25% (w/v) suspension in corn oil) was administered by gavage at a dose of 4,556, 6,834, or 10,250 mg/kg body weight. Dosing was followed by a 14-day observation period. None of the animals died during the study, and there was no evidence of significant adverse effects. However, hypoactivity and ruffled fur were observed in all dose groups, and labored breathing and diuresis were observed in the highest dose group. The animals had returned to normal by day 2, and gross pathological alterations were not observed at necropsy. It was concluded that the LD₅₀ was > 10,250 mg/kg body weight.2

Dermal

An acute dermal toxicity study was performed using groups of 4 rabbits (non-GLP study; ages and strain not stated). Pentaerythritol tetra-di-t-butyl hydroxyhydrocinnamate (dose of 100, 316, 1,000, or 3,160 mg/kg body weight, in corn oil) was applied for 24 h, under occlusion (nonabsorbent paper backing), to clipped abdominal skin. In each dose group, the test sites were abraded (2 rabbits) and remained intact (2 animals); the trunk was wrapped with gauze and adhesive tape. The animals were observed for mortality and signs of toxicity for up to 14 days post-dosing. Behavior, appearance, and body weight gain were normal for all animals throughout the study, and none of the animals died. Slight erythema was observed in all animals at the end of exposure. Reactions completely subsided between days 2 and 5 and were not observed at study termination. Gross pathologic findings were not observed at necropsy. It was concluded that the LD₅₀ was > 3,160 mg/kg body weight.

Repeated Dose Toxicity

In a repeated dose toxicity study, pentaerythritol tetra-di-t-butyl hydroxyhydrocinnamate was administered (in food) to groups of 12 beagle dogs (males and females; 24 to 31 weeks old) for 3 months. The 3 groups were fed the test material at concentrations of 1,000, 3,000, and 10,000 ppm, respectively. At the end of 3 months, 1 animal per sex per dose was fed the control diet for an additional 4 weeks. There was no evidence of clinical symptoms or signs of systemic toxicity in any of the animals. Food consumption, body weight gain, and mean food conversion were unaffected by treatment. The results of ophthalmic examinations did not indicate any treatment-related changes, and there was no evidence of auditory perception impairment. Urinalyses and hematologic and blood chemistry evaluations were unremarkable. An increase in total bilirubin concentration was noted at weeks 4 and 9, but not at week 13. This observation was considered incidental and of no toxicological significance, because there were no changes in other bilirubin-linked parameters. Organ weights and ratios for treated animals were comparable to control values. No treatment-related macroscopic or microscopic changes were observed. It was concluded that no treatment-related adverse effects were observed in this study.2

Skin Sensitization

The skin sensitization potential of a pentaerythritol tetra-di-t-butyl hydroxyhydrocinnamate (0.5% w/v) solution in dimethyl phthalate was evaluated using human subjects (number and ages not stated).2 Details relating to the test protocol were not included. The test substance was classified as a non-sensitizer.

REPRODUCTIVE AND DEVELOPMENTAL TOXICITY

In a reproductive toxicity study, groups of male and female rats of the Crj: CD(SD) strain (6 weeks old; number per group not stated) were fed pentaerythritol tetra-di-t-butyl hydroxyhydrocinnamate in the diet at concentrations of 1,000, 3,000, and 10,000 ppm, respectively, continuously throughout 2 generations.2 A fourth group was fed a control diet. The animals were maintained on their respective diets for 10 weeks prior to mating. F₀ parents were killed after weaning of the F₁ litters, and organ weight analysis and preservation of tissues was performed on all parents. The F₁ generation comprised 24 male and 24 female pups. A male pup and female pup from each litter were selected for organ weight analysis and the remaining animals were killed and examined macroscopically. The same procedure for feeding and mating F₀ parents was used for F₁ generation animals.

None of the animals (F₀ or F₁ parents) died, and there were no consistent effects that were considered treatment-related, which included: no clinical signs of toxicity, or changes in mating performance, pregnancy rate, and duration of
gestation. There were also no remarkable findings at terminal necropsy. In evaluating toxicity to offspring (F₀ or F₁), no adverse effects on litters that may have resulted from parental dosing with pentaerythrityl tetra-di-t-butyl hydroxyhydrocinnamate were observed. Particularly, there were no adverse effects on litter size, pup weights, sex ratio, or pup mortality. At terminal necropsy, a slightly faster growth rate was apparent among offspring (both generations) associated with the 10,000 ppm dietary level. This observation appeared to have been independent of litter size, and was confirmed by the noticeably higher mean litter weight in this group at termination. A no-observed-adverse-effect-level (NOAEL) of 10,000 ppm pentaerythrityl tetra-di-t-butyl hydroxyhydrocinnamate was reported for parents and their F₁ and F₂ offspring.²

The developmental toxicity/teratogenicity potential of pentaerythrityl tetra-di-t-butyl hydroxyhydrocinnamate was evaluated using 3 groups of 25 female Sprague-Dawley rats (ages not stated).² Females were mated in a ratio of 1 male per 3 females. The 3 groups then received oral doses (gavage) of 150, 500, and 1,000 mg/kg daily on days 6 through 15 of gestation. The dams were necropsied and fetuses were removed by Caesarean section on day 21 of pregnancy. At low and intermediate doses, an increase in food consumption was noted during the treatment period. However, there was no apparent effect on body weight gain. The rates of implantation and resorptions were comparable in all groups, and the same was true for the average weights of the fetuses. There were no treatment-related effects on embryonic development. However, phalangeal nuclei of the hind limb and calcanei displayed higher rates of ossification (when compared to control; group not defined) in both low and intermediate dose groups, but not in the high dose group. It was stated that this effect on physiological growth may be associated with the increased food consumption noted for dams that received low and intermediate doses. An NOAEL (maternal and fetal) of 1,000 mg/kg body weight was reported. Pentaerythrityl tetra-di-t-butyl hydroxyhydrocinnamate did not induce teratogenic effects or maternal toxicity in this study.

In another study, the developmental toxicity/teratogenicity of pentaerythrityl tetra-di-t-butyl hydroxyhydrocinnamate was evaluated using 3 groups of 30 female NMRI mice (ages not stated).² The 3 groups received oral doses of 150, 500, and 1,000 mg/kg body weight in accordance with the protocol in the preceding study. There was no evidence of treatment-related maternal toxicity. Body weight gain and food consumption were comparable for the 3 groups. The rates of implantation and resorptions were also comparable in all groups, and the same was true for the average weights of the fetuses. Skeletal assessment results indicated minor deviations (compared to control; group not defined) in the low and high dose groups. In the low dose group, the incidences of phalangeal nuclei of the hind limb and calcanei were significantly different when compared to the control group. An increase in the number of incompletely ossified sternebrae was observed in the highest dose group. Due to the absence of dose-relationships and considering that incidences generally display great variability, it was noted that no special significance should be associated with these findings. An NOAEL (maternal and fetal) of 1,000 mg/kg body weight was reported. It was concluded that pentaerythrityl tetra-di-t-butyl hydroxyhydrocinnamate was non-teratogenic in this study.

**GENOTOXICITY**

**In Vitro Assays**

The genotoxicity of pentaerythrityl tetra-di-t-butyl hydroxyhydrocinnamate (in DMSO) was evaluated in the Ames test using the following *Salmonella typhimurium* strains, with and without metabolic activation: TA98, TA100, TA1535, and TA1537.² The test substance was evaluated at concentrations up to 250 µg/0.1 ml (without activation) and up to 100 µg/0.1 ml (with activation). The following positive controls were used: N-methyl-N'-nitro-N-nitrosoguanidine (for strain TA1535), 9(5)-aminoacridine hydrochloride monohydrate (for strain TA1537), daunoblastin (for strain TA98), and 4-nitroquinoline-n-oxide (for strain TA100). There was no increase in the number of reverse mutations either with or without metabolic activation, and the test substance was classified as negative for genotoxicity.² In another Ames test, pentaerythrityl tetra-di-t-butyl hydroxyhydrocinnamate was evaluated at doses up to 5,000 µg/plate, with and without metabolic activation, using the following *Salmonella typhimurium* strains: TA98, TA100, TA1535, TA1537, and TA1538. Positive controls were not mentioned. Results were negative with and without metabolic activation.²

**In Vivo Assays**

A dominant lethal genotoxicity study of pentaerythrityl tetra-di-t-butyl hydroxyhydrocinnamate was performed using groups of 20 male NMRI mice (ages not stated), and a limited number of female mice used for mating (details in following protocol).² The test substance, in aqueous carboxymethylcellulose (CMC), was administered by gavage to 2 groups of males at single doses of 1,000 and 3,000 mg/kg (dose volume = 0.2 ml/kg body weight), respectively. Negative controls received vehicle only, and a positive control group was not included in the study. After dosing, the males were mated with females, and each group consisted of 20 males caged with 2 untreated females. After 1 week, the 2 females per
group were replaced with 2 other females. This protocol was continued for 6 consecutive weeks of mating. Pregnant females were necropsied on day 14 of pregnancy. The number of live embryos and embryonic deaths was recorded, and uteri were examined for early embryonic resorptions. There were no differences in the mating ratio, number of implantations, or embryonic deaths between test and control groups. It was concluded that there was no evidence of dominant lethal effects in the study.

Groups of male and female hamsters (ages and number per group not stated) received doses of 500, 1,000, and 2,000 mg/kg pentaerythritol tetra-di-t-butyl hydroxyhydrocinnamate in 0.5% CMC, by gavage, daily for 2 days. The test substance and controls were administered at a dose volume of 20 ml/kg. Cyclophosphamide (in 0.5% CMC, 128 mg/kg) and 0.5% CMC served as positive and vehicle controls, respectively. At 24 h after the second dose, the animals were killed and bone marrow was removed from the femur. Bone marrow cells (1,000 per animal) were scored for chromosomal abnormalities, and the following anomalies were reported: single Jolly bodies, fragments of nuclei in erythrocytes, micronuclei in erythroblasts, micronuclei in leucopoietic cells, and polyploidy cells. For all dose groups, the percentage of cells with anomalies of the nuclei did not differ significantly when compared to negative controls. It was concluded that the test substance was non-mutagenic.

In another genotoxicity study of pentaerythritol tetra-di-t-butyl hydroxyhydrocinnamate, male and female hamsters (ages and number per group not stated) were dosed (same doses) according to the preceding test protocol. Sodium CMC and cyclophosphamide served as vehicle and positive controls, respectively. Animals were injected with colcemide 2 h after administration of the second dose and killed 4 h later. Bone marrow was obtained from the femur. The following aberrations were reported: chromatid-type aberrations, chromosome-type aberrations, chromatid gaps, and chromosome pulverations. Aberrations were not detected in chromosome displays from negative control, intermediate dose, and high dose groups. In low dose animals, one metaphase per 400 cells with chromatid-type aberrations (breaks) was detected. However, this incidence was within the frequency observed in historical controls and was considered spontaneous in origin. It was concluded that the test substance was non-mutagenic.

In the micronucleus assay, a 5,000 mg/kg dose of pentaerythritol tetra-di-t-butyl hydroxyhydrocinnamate was administered orally to male and female rats (number of animals, ages, and strain not stated) over an exposure period of up to 66 h. Details relating to the test protocol and study results were not included. There was no evidence of systemic toxicity, and the test substance was classified as negative for genotoxicity.

**CARCINOGENICITY**

The carcinogenicity of pentaerythritol tetra-di-t-butyl hydroxyhydrocinnamate was evaluated using groups of male and female Sprague-Dawley rats (ages and number per group not stated). The groups were fed the test substance at dietary concentrations of 1,000, 3,000, and 10,000 ppm for 104 weeks. The control group used in the study was not defined, and details relating to the test protocol and study results were not included. It was noted that there was no evidence for a tumorigenesis potential in the rat in this study. In another carcinogenicity study, groups of mice (strain and number per group not stated) were fed pentaerythritol tetra-di-t-butyl hydroxyhydrocinnamate in the diet at concentrations of 100, 300, and 1,000 ppm for 24 months. The control group used in the study was not defined, and details relating to the test protocol and study results were not included. It was noted that there was no evidence for a tumorigenesis potential in the mouse in this study.

**SUMMARY**

Pentaerythritol tetra-di-t-butyl hydroxyhydrocinnamate functions as an oxidant in cosmetic products. According to information on the use of this ingredient supplied to FDA by industry as part of the VCRP in 2013, this ingredient was being used in 622 products. The Personal Care Products Council conducted a survey of ingredient use concentrations in 2013, and the results indicated use of this ingredient at concentrations up to 0.8%. Pentaerythritol tetra-di-t-butyl hydroxyhydrocinnamate is an FDA-approved indirect food additive, and, depending on its use in food contact surfaces, has been limited to concentrations as low as 0.1%.

In an acute inhalation toxicity study, rats were exposed (nose-only) to pentaerythritol tetra-di-t-butyl hydroxyhydrocinnamate at concentrations up to 1,951 mg/m³ of air. Slight, transient dyspnea was reported, and no pathological changes were observed at necropsy. An LD₅₀ > 10,250 mg/kg body weight was reported in an acute oral
toxicity study involving rats. There were no gross pathological alterations at necropsy. An LD$_{50}$ > 3,160 mg/kg body weight was reported in an acute dermal toxicity study involving rabbits. Again, there were no gross pathological findings at necropsy.

In a repeated dose toxicity study, no treatment-related macroscopic or microscopic changes were observed in rats that received oral doses (in feed) at concentrations up to 10,000 ppm.

Pentaerythritol tetra-di-t-butyl hydroxyhydrocinnamate (0.5% w/v solution in dimethyl phthalate) was classified as a non-sensitizer in human subjects.

An NOAEL of 10,000 ppm pentaerythritol tetra-di-t-butyl hydroxyhydrocinnamate was reported for parents and their F$_1$ and F$_2$ offspring in an oral reproductive toxicity study involving rats. In oral developmental toxicity/teratogenicity studies involving rats and mice, an NOAEL (maternal and fetal) of 1,000 mg/kg body weight was reported for pentaerythritol tetra-di-t-butyl hydroxyhydrocinnamate.

In the in vitro Ames test, pentaerythritol tetra-di-t-butyl hydroxyhydrocinnamate was not genotoxic at doses up to 5,000 µg/plate in Salmonella typhimurium strains. In an in vivo dominant lethal genotoxicity study, results were negative for pentaerythritol tetra-di-t-butyl hydroxyhydrocinnamate in mice at doses up to 3,000 mg/kg body weight. Results for the test substance were also negative for chromosomal aberrations in hamsters that received oral doses up to 2,000 mg/kg body weight, and in a micronucleus assay in which rats were dosed orally with 5,000 mg/kg body weight.

Reportedly, there was no indication of tumorigenic potential in 2-year carcinogenicity studies on pentaerythritol tetra-di-t-butyl hydroxyhydrocinnamate involving rats (oral doses up to 10,000 ppm in feed) and mice (oral doses up to 1,000 ppm in feed).

Toxicokinetic data on pentaerythritol tetra-di-t-butyl hydroxyhydrocinnamate were not identified in the published literature.
Table 1. Properties of Pentaerythritol Tetra-di-t-Butyl Hydroxyhydrocinnamate.  

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Density</td>
<td>1.15 g/cm³</td>
</tr>
<tr>
<td>Water Solubility (mg/L @ 25°C)</td>
<td>2.3 x 10⁻¹⁶ (estimated)</td>
</tr>
<tr>
<td>Stability in Water (hydrolysis) (t₁/₂)</td>
<td>2.1 years</td>
</tr>
<tr>
<td>Vapor Pressure (hPa at 25°C)</td>
<td>7.1 x 10⁻³¹ (estimated)</td>
</tr>
<tr>
<td>Melting Point (°C)</td>
<td>115 to 118</td>
</tr>
<tr>
<td>Boiling Point (°C)</td>
<td>1130 (estimated)</td>
</tr>
<tr>
<td>Flash Point (°C)</td>
<td>297</td>
</tr>
<tr>
<td>Autoflammability (°C)</td>
<td>&gt;350</td>
</tr>
<tr>
<td>Log K_{ow}</td>
<td>23.0 (estimated)</td>
</tr>
<tr>
<td>Indirect (OH⁻) Photodegradation Half-life (t₁/₂)</td>
<td>1.2 hours</td>
</tr>
</tbody>
</table>

Table 2. Frequency and Concentration of Use According to Duration and Type of Exposure for Pentaerythritol Tetra-di-t-Butyl Hydroxyhydrocinnamate.  

<table>
<thead>
<tr>
<th>Exposure Type</th>
<th># of Uses</th>
<th>Conc. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eye Area</td>
<td>75</td>
<td>0.24-0.8</td>
</tr>
<tr>
<td>Incidental Ingestion</td>
<td>219</td>
<td>0.1-0.8</td>
</tr>
<tr>
<td>Incidental Inhalation - Sprays</td>
<td>64</td>
<td>Sprays: 0.05-0.44; 0.0004-0.1²</td>
</tr>
<tr>
<td>Incidental Inhalation - Powders</td>
<td>12</td>
<td>Powders: 0.01-0.014; 0.01-0.34³</td>
</tr>
<tr>
<td>Dermal Contact</td>
<td>380</td>
<td>0.0001-0.8</td>
</tr>
<tr>
<td>Deodorant (underarm)</td>
<td>NR</td>
<td>Sprays: 0.00075-0.024</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Not Sprays: 0.0005-0.11</td>
</tr>
<tr>
<td>Hair - Non-Coloring</td>
<td>11</td>
<td>0.00001-0.1</td>
</tr>
<tr>
<td>Hair-Coloring</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Nail</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Mucous Membrane</td>
<td>263</td>
<td>0.02-0.8</td>
</tr>
<tr>
<td>Baby Products</td>
<td>1</td>
<td>0.01-0.028</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Duration of Use</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Leave-On</td>
<td>553</td>
<td>0.0001-0.8</td>
</tr>
<tr>
<td>Rinse off</td>
<td>65</td>
<td>0.00001-0.5</td>
</tr>
<tr>
<td>Diluted for (bath) Use</td>
<td>4</td>
<td>0.2</td>
</tr>
</tbody>
</table>

Totals***/Conc. Range: 622 0.00001-0.8

NR = Not Reported; Totals = Rinse-off + Leave-on Product Uses

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

2. It is possible that these products may be sprays, but it is not specified whether the reported uses are sprays.

3. It is possible that these products may be powders, but it is no specified whether the reported uses are powders.
References


